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Pathology

EXPERIMENTAL PATHOLOGY

1175. 3:4-Benzpyrene in the Smoke of Cigarette Paper, Tobacco, and Cigarettes

S. Z. CARDON, E. T. ALVORD, H. J. RAND, and R. HITCHCOCK. *British Journal of Cancer [Brit. J. Cancer]* 10, 485-497, Sept., 1956. 12 figs., 12 refs.

In this report from the Rand Development Corporation, Cleveland, Ohio, an apparatus is described in which tobacco and cigarette paper were burned, separately and together, at temperatures similar to those obtaining during smoking, the resulting tars being analysed for 3:4-benzpyrene and other possible carcinogens. 3:4-Benzpyrene was identified in the tars from the smoke of cigars, cigarettes, tobacco, and cigarette paper on the basis of: (1) fluorescence spectra, (2) ultraviolet light absorption spectra, (3) chemical analysis involving iodination of purified tar fractions, and (4) recovery of added 3:4-benzpyrene after identical purification procedures. 1:2-Benzpyrene was also thought to be present. The quantity of the carcinogen obtained from burning one cigarette completely is estimated as 0.16 μ g. (0.04 μ g. from the paper and 0.12 μ g. from the tobacco). In smoking, one-fifth to one-quarter of the cigarette is normally discarded as the butt.

P. Mestitz

1176. The Inhibition of Formation of 3:4-Benzpyrene in Cigarette Smoke

E. T. ALVORD and S. Z. CARDON. *British Journal of Cancer [Brit. J. Cancer]* 10, 498-503, Sept., 1956. 4 figs., 1 ref.

In a further report from the Rand Development Corporation, Cleveland, Ohio [see Abstract 1175] the authors report that treatment of cigarette paper and tobacco with ammonium compounds of strong acids, such as the phosphate, sulphate, sulphamate, or chloride, reduced the formation of 3:4-benzpyrene in the smoke by as much as 50%.

P. Mestitz

1177. The Delayed Type of Allergic Reaction in Cancer: Altered Response to Tuberculin and Mumps Virus

J. LOGAN. *New Zealand Medical Journal [N.Z. med. J.]* 55, 408-410, Oct., 1956. 9 refs.

Continuing his study of cutaneous anergy in cancer, the author carried out skin tests with mumps virus vaccine on 73 patients with carcinoma and 28 patients with malignant lymphoma [no clinical details given] at Wellington Hospital, New Zealand. The incidence (82%) of a positive reaction in 33 cases of early carcinoma

did not differ significantly from that in the normal urban population; however, 27 (71%) of 38 patients with carcinoma in the later stages failed to react, and the reactions in those who did were weaker than normal. A similar lack of response was observed in 12 (81%) out of 15 cases in the late stages of malignant lymphoma.

In Mantoux tests with 1 in 1,000 and 1 in 10,000 tuberculin on 29 patients with carcinoma no significant difference from the normal distribution of responses was found. In contrast, none of 8 patients with malignant lymphoma gave a positive result. From these results and from those of others reported in the literature the author concludes that in malignant lymphoma there is a general depression of the delayed type of allergic response, whereas in advanced carcinoma the lack of response to mumps virus vaccine alone is probably due to exhaustion of the leucocyte sensitizing factor for that virus, but not for tuberculin.

J. B. Cavanagh

1178. The Effect of Negatively Ionized Air on the Cold Receptors of the Skin. (Влияние отрицательно ионизированного воздуха на холодовую рецепцию кожи)

M. V. BUSYGINA and A. A. MINKH. *Гигиена и Санитария [Gigiena]* 5-11, No. 12, Dec., 1956. 3 figs., 16 refs.

In view of previously observed effects of atmospheric ionization on the human subject and its possible bearing on the value of health resorts, the authors have investigated the effect of ionized air quantitatively, using the cold receptors of the skin as an indicator, Snyakin having shown that variation in the number of functioning receptors could be used in this way to determine the response of the organism to changes in the environment.

The experiments were performed on 14 healthy adults in whom the number of functioning cold receptors in one sq. cm. of skin on the inner aspect of the forearm was first determined by means of a thermo-aesthesiometer, this being repeated at intervals of a few minutes for a period of 15 to 20 minutes. Next, 10 cold receptors were identified, their positions marked, and the number which were functioning at any one time was determined each minute for 5 minutes. Both methods were employed in each case, the first method giving an index of the sensitivity of the skin to cold, while the second reflected the behaviour of individual receptors to changes in the environment. All the tests were carried out under conditions of constant temperature and humidity. Readings were made both before and after exposure of

the subject, first to non-ionized air moving at a velocity of 1.2 m. per second, and then to ionized air moving at the same velocity. It was found that the initial mean number of receptors per sq. cm. of skin was 6.1, this increasing to 9.5 after exposure to non-ionized air, and diminishing to 3.6 after exposure to negatively ionized air.

In another series of experiments designed to demonstrate the effect of changes of temperature the number of active receptors was determined first in an environmental temperature of 20° C., then at 23° C., and once more at 20° C. This was repeated in negatively ionized air. A rise in temperature in ordinary air caused a marked reduction in the number of receptors, a fall in temperature having a contrary effect; but in ionized air the change in the number of receptors was insignificant.

The authors conclude that exposure to ionized air leads to a marked reduction in the number of functioning cold receptors, compared with that in normal air moving at the same velocity. This reduction is due to inhibition at the central end of the receptor. The occurrence of drowsiness in subjects exposed to ionized air suggests that a lowering of the general level of activity of the organism is induced by the development in the cerebral cortex of a protective inhibitory state which evidently affects reflex activity.

Basil Haigh

1179. **Experimental Hypertension Induced by Narrowing of the Lumen of the Inferior Vena Cava.** (Экспериментальная гипертония, вызванная сужением просвета воротной вены)

F. A. МОРОКНОВ. *Архив Патологии* [Ark. Patol.] 18, 54-58, No. 7, 1956. 3 figs., 12 refs.

In studies in experimental hypertension carried out at Yaroslav Medical Institute partial ligation of the inferior vena cava resulting in at least 60% narrowing of the lumen was performed on 7 adult dogs. All animals developed arterial hypertension which lasted for weeks and in some cases even months. Control operations, without actual ligation of the vein, produced a transient rise in blood pressure which, however, lasted not more than 24 to 48 hours. Since ligation of the inferior vena cava leads to ischaemia of the greater portion of the intestine, liver, spleen, and other organs, the author argues that a mechanism similar to that of the Goldblatt kidney may be responsible, and suggests that the kidneys may not be unique in their ability to produce vasopressive substances in response to ischaemia. He supports his argument by quoting similar Russian experiments involving the uterus and heart.

A. Swan

1180. **Further Studies on the Plasma Lymphocytosis Stimulating Factor in Chronic Lymphatic Leukaemia and Some Other Disease States**

D. METCALF. *British Journal of Cancer* [Brit. J. Cancer] 10, 431-441, Sept., 1956. 2 figs., 10 refs.

On the basis of a previous finding that the intracerebral injection of plasma from the majority of patients with chronic lymphatic leukaemia would cause a rise in the number of circulating lymphocytes in suckling mice, the author has investigated, at the Walter and Eliza Hall Institute of Medical Research, Melbourne, the effect of

plasma from patients with other haematological disorders and various neoplastic conditions. It was found that only the plasma from patients with lymphosarcoma or myelofibrosis produced a similar lymphocytosis.

The lymphocytosis-stimulating factor in the plasma of these patients was found to decrease following transfusions of whole blood or during clinical remissions of the disease. The intramuscular injection of adrenaline increased the stimulating activity of plasma, and this effect was not annulled by splenectomy but was inhibited when the patients were treated with cortisone. The lymphocytotic effect of active plasma was also inhibited in the mice by the concurrent administration of cortisone or oestrogens. The factor is thermolabile, being destroyed when the plasma is heated to 60° C. for 15 minutes, but it withstands freeze-drying.

G. Calcutt

1181. **The Thymic Origin of the Plasma Lymphocytosis Stimulating Factor**

D. METCALF. *British Journal of Cancer* [Brit. J. Cancer] 10, 442-457, Sept., 1956. 3 figs., 16 refs.

The author has shown that plasma from patients with chronic lymphatic leukaemia, lymphosarcoma, or myelofibrosis can induce lymphocytosis in infant mice [see Abstract 1180]. In order to identify the organ responsible for this effect various organs obtained at necropsy from normal subjects and patients with the above diseases were extracted in saline and tested. It was shown that the thymus and thyroid glands from normal human subjects and from mice exhibited lymphocytotic activity (the thyroid only slightly), as did also the thymus and thyroid glands, plasma, and serum from human patients or mice suffering from chronic lymphatic leukaemia. Tissue-culture studies confirmed that the active principle was formed in the epithelial-type cells of the thymus. Evidence is adduced to show that the thymus gland is the organ responsible for the experimental findings obtained with plasma from cases of the disease. The results are considered in relation to clinical and pathological data.

G. Calcutt

1182. **The Hormonal Production of Nephrosclerosis and Periarthritis Nodosa in the Primate**

H. SELYE and P. BOIS. *British Medical Journal* [Brit. med. J.] 1, 183-186, Jan. 26, 1957. 13 figs., 14 refs.

Experiments were carried out at the University of Montreal on 8 young female monkeys from which the right kidney had been removed under sterile conditions. Four such animals received daily average doses of 7.5 mg. of 2-methyl-9(α)-fluorocortisol (Me-F-COL), a highly potent synthetic mineralocorticoid, in the form of microcrystals in aqueous suspension subcutaneously, 2 were subjected to adrenalectomy and then received daily doses of 2 to 8 mg. of Me-F-COL, while 2 served as controls. Both adrenalectomized animals died about the 10th day after operation, the pathological findings being characterized by acute cardiovascular damage and leucocytic infiltrations, especially in the liver and kidneys. The other 6 monkeys were killed on the 80th day. In all 4 animals which had received the drug severe malignant

hyalinizing nephrosclerosis was present, together with cardiovascular changes, including widespread periarteritis nodosa. There were no complicating signs of the periodic paralysis characteristic of primary aldosteronism, and no apparent relationship to allergic hypersensitivity.

[This work is of great importance since the chemical used is one of the most active mineralocorticoids. The changes described indicate that much work remains to be done before this substance can be introduced into clinical practice.]

G. B. West

CHEMICAL PATHOLOGY

1183. Micro Determination of Histamine in Biological Fluids. [In English]

J. A. H. GOOSZEN, T. H. STRENGERS, and J. DONKER. *Acta allergologica [Acta allerg. (Kbh.)]* 10, 113-118, 1956. 3 figs., 1 ref.

For accurate determination by Code's method of the blood histamine level in human beings 20 ml. of blood is required. In this paper a micro-modification of Code's method is described in which 2 ml. of blood is sufficient for accurate histamine assay. It is shown that statistically there is no difference in accuracy between the level as determined by Code's method and that determined by the micro method.

[The description of the apparatus and of the method employed should be read in full by those interested.]

A. W. Frankland

1184. The Practical Application of the Rapid Intravenous Glucose Tolerance Test in Various Disease States Affecting Glucose Metabolism

D. S. AMATUZIO, E. D. RAMES, and S. NESBITT. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* 48, 714-720, Nov., 1956. 1 fig., 24 refs.

The authors describe from the University of Minnesota, Minneapolis, a simple intravenous glucose tolerance test which is suitable for routine use. The patient is given an adequate diet containing at least 150 g. of carbohydrate daily for 7 or more days before the test. After the fasting blood sugar level has been determined he is then given an intravenous infusion over 4 minutes of 25 g. of glucose as a 30% solution in distilled water, and 68 minutes later capillary blood is withdrawn for glucose estimation. The blood glucose value in mg. per 100 ml. is expressed as the excess of the 68-minute value over the fasting value. For children a dose of 0.5 g. of glucose per kg. body weight may be given.

The test was carried out on 103 normal male subjects aged 25 to 50 years and on 283 patients, of whom 39 were diabetics. In the normal subjects the glucose excess ranged from -28 to +26 mg. (mean $+4.6 \pm 12.1$ mg.) per 100 ml. When the test was repeated on 20 of the normal subjects the results showed no significant differences. For the diabetic patients the range was +20 to +102 mg. (mean $+50.4$ mg.) per 100 ml., only one showing a value below 26 mg. per 100 ml. For patients with hepatic cirrhosis, viral hepatitis, inflammatory

diseases of various types, uraemia, obesity, or malnutrition the glucose excess at 68 minutes exceeded 20 mg. per 100 ml. in most cases and there was a considerable gap between the values for these groups and that for the normal subjects, the mean value of the glucose excess being significantly raised in each group except in 15 cases of untreated hyperthyroidism, in which the results fell within the normal range.

The standard 100-g. oral glucose tolerance test was then performed on 115 normal subjects. The maximum value was the same at 30 minutes and at 60 minutes and was only 120 mg. per 100 ml. in 40 subjects (34%); all blood glucose values were below 110 mg. per 100 ml. at 120 minutes. The intravenous and oral tests were compared in 15 patients with mild diabetes and 14 patients with hyperthyroidism. In all the diabetics the intravenous test gave an abnormal result, while in 4 the oral test gave a normal result. In the hyperthyroid group all intravenous tests gave a normal result, but only 9 of the oral tests did so.

The authors consider values for glucose excess greater than 26 mg. per 100 ml. at 68 minutes to be abnormal. They point out that in the interpretation of abnormal glucose tolerance test results it should not be overlooked that inflammation, uraemia, active liver disease, malnutrition, and obesity may be responsible for the abnormality.

M. Lubran

1185. A Clinical Evaluation of the C-Reactive Protein Test

R. S. YOCUM and A. A. DOERNER. *A.M.A. Archives of Internal Medicine [A.M.A. Arch. intern. Med.]* 99, 74-81, Jan., 1957. 15 refs.

This paper consists essentially of a record of the results of the routine performance of the C-reactive protein test on 1,262 occasions on 729 patients admitted to the U.S. Public Health Service Hospital, San Francisco, with 123 different clinical diagnoses. In tabulating the results the authors group their cases in seven diagnostic categories.

Positive results were found during the acute phase in nearly all infectious bacterial diseases, with less frequent positive results in viral diseases and the more chronic infections. A positive reaction tended to be present in infections associated with gastro-intestinal disease and diabetes, severe congestive heart failure usually with mild pulmonary infection, acute coronary insufficiency, pulmonary infarction, acute rheumatic fever, rheumatoid arthritis, penicillin-sensitivity reactions, and malignant conditions with metastases, and during the first 24 to 48 hours after a major surgical procedure. A negative result is particularly noted as usual in acute infective hepatitis, cerebral thrombosis, and destructive lesions of the central nervous system. The authors consider that the test is more "sensitive" than the erythrocyte sedimentation rate in the presence of inflammatory or necrotic processes.

[It is difficult to deduce any "evaluation" of this test from this report, which is fundamentally a record of experience on a wide and general basis.]

Harry Coke

1186. Identification of Bacterial Residues in Sarcoid Lesions

S. E. NETHERCOTT and W. G. STRAWBRIDGE. *Lancet* [Lancet] 2, 1132-1134, Dec. 1, 1956. 2 figs., 13 refs.

Attempts to demonstrate tubercle bacilli in sarcoid lesions, and so to show sarcoidosis to be a manifestation of tuberculosis, have so far failed. But the search for bacterial residues of previous tuberculous infection has been more successful. In the present study portions of tissue containing sarcoid lesions from 4 patients have been examined at the Welsh National School of Medicine, Cardiff, for bacterial residues. The tissue was first autoclaved to remove collagen and then acid-hydrolysed; the amino-acids in the hydrolysate were separated by paper chromatography and electrophoresis. α : ϵ -Diaminopimelic (DAP) acid appeared on the chromatophoretogram and mycolic acid was identified in the humins separated from the hydrolysate. Mycolic acid was confirmed by comparing its infrared absorption spectrum with that of wax C obtained from tubercle bacilli. Since DAP and mycolic acids are not normal constituents of the body but are found in human strains of tubercle bacilli, it is suggested that sarcoidosis may be a manifestation of tuberculosis.

J. E. Page

HAEMATOLOGY

1187. The Bone Marrow in Malignant Disease

E. M. K. PILLERS, J. MARKS, and J. S. MITCHELL. *British Journal of Cancer* [Brit. J. Cancer] 55, 458-471, Sept., 1956. 5 figs., 25 refs.

The authors of this paper from the University of Cambridge analyse the findings on examination of sternal bone marrow from 601 patients suffering from malignant disease at various sites, including the breast (195 cases), the bronchus (125 cases), and the cervix uteri (61 cases). Smears prepared by the usual technique and marrow flecks picked out from oxalated specimens and spread on slides were examined. The marrow was classified as: (1) positive, if definite malignant cells were found; (2) suspicious, if there was a definite plasmacytosis, often with general marrow hyperplasia; and (3) negative, if no abnormal cells or bone-marrow reactions were detected. Malignant cells were found in 37 cases (the site of the primary neoplasm being the breast in 12, the lung in 14, ovary in 2, cervix in one, alimentary canal in one, urinary tract in one, and unknown in 6). The changes were regarded as suspicious in 180 cases, while in 384 no change was detected. It has been suggested that eosinophilia in the marrow indicates malignancy, but in the present series no definite correlation was found between marrow eosinophilia and other changes.

The average survival time of patients with carcinoma of the bronchus was 5 months when the bone-marrow findings were positive, 6 months when they were suspicious, and 7 months when they were negative. The survival time of patients with carcinoma of the cervix was significantly longer with a negative marrow than with either a positive or a suspicious bone marrow. In

patients with carcinoma of the breast no correlation was observed between survival time and the bone-marrow findings.

The authors point out that in cases without definite evidence of malignancy the bone-marrow appearances are often suspicious. A search should always be made for the cause of a plasmacytosis of this type; plasmacytosis is not pathognomonic of malignant disease alone, since it is observed in other conditions.

M. C. G. Israëls

1188. The Bone Marrow in Ischaemia

D. A. SUGERMAN. *Medical Journal of Australia* [Med. J. Aust.] 2, 913-917, Dec. 22, 1956. Bibliography.

A review of the literature indicates that the stimulating effect of anoxia on erythropoiesis is produced not by a direct action on the bone marrow, but through a hormonal intermediary. At the Royal Melbourne Hospital, the author examined marrow specimens from 11 limbs (the lower end of the femur and the upper and lower ends of the tibia) which had been amputated because of ischaemic changes due to peripheral vascular disease. Supporting evidence of disease was obtained from radiographs in 3 and anatomically by dissection in 6 of these cases. The ages of the patients ranged from 52 to 82 years. Full details, including the haemoglobin level and bone-marrow findings, are given in a table. Intermittent claudication was present in 5 cases, atheroma of the femoral or popliteal artery with or without calcification in 4, and a femoral embolus in one. Most of the patients had slight to moderate emphysema.

In 2 control limbs without arterial disease no evidence of erythropoiesis was found. In the present series active erythropoiesis in the lower part of the femur was observed only in one cyanosed patient with severe emphysema and atheroma of the femoral artery with narrowing of the popliteal and posterior tibial arteries. In none of the tibias examined was there active erythropoiesis. A possible explanation is that the marrow anoxia exceeded a critical level, beyond which the anoxic stimulus lost its effect on the bone marrow. The author considers, however, that in view of the number of limbs examined and the variations in the clinical and pathological findings a more likely explanation is that ischaemia does not directly stimulate the bone marrow.

The investigation also showed that no erythropoiesis-stimulating hormone is formed in stagnant blood in a limb, and that bone-marrow ischaemia is not concerned in the pathogenesis of polycythaemia vera.

F. Hillman

1189. An Analysis of Errors Detected in the Course of Large Scale ABO Grouping. [In English]

C. C. BOWLEY and I. DUNSFORD. *Vox sanguinis* [Vox Sanguinis (Amst.)] 1, 250-254, Nov., 1956. 1 ref.

1190. Studies on the Clot-promoting Activity of Glass

E. SHAFRIR and A. DE VRIES. *Journal of Clinical Investigation* [J. clin. Invest.] 35, 1183-1190, Nov., 1956. 29 refs.

1191. Studies on Spontaneous *in vitro* Autohemolysis in Hemolytic Disorders

L. E. YOUNG, M. J. IZZO, K. I. ALTMAN, and S. N. SWISHER. *Blood [Blood]* 11, 977-997, Nov., 1956. 3 figs., 31 refs.

The authors give details of more than 100 careful studies carried out *in vitro* at the University of Rochester School of Medicine and Dentistry, New York, on the rate of autohaemolysis of defibrinated blood incubated at 37° C. for 48 hours. A total of 64 samples of normal blood were first tested and from the results a normal range was established, the effect of various technical factors, such as how the blood was mixed, being also studied. In some of the experiments additional glucose or adenosine or other nucleoside was added to the blood before incubation.

In blood from patients with hereditary spherocytosis accelerated haemolysis was constantly present. However, the phenomenon is not confined to this disorder, as it was observed in other types of spherocytosis and in several examples of non-spherocytic haemolytic anaemia. In hereditary spherocytosis the accelerated haemolysis was closely correlated with the abnormal increase in osmotic fragility which takes place on incubating blood for 24 hours at 37° C. Both tests seemed equally sensitive in detecting hereditary spherocytosis. The addition of adenosine, guanosine, or inosine to the blood caused moderate to marked reduction in autohaemolysis of nearly all the types of erythrocyte tested, and the addition of glucose regularly and markedly inhibited autohaemolysis of the cells in hereditary spherocytosis. However, in auto-immune haemolytic disease and in myeloid metaplasia it was found that the addition of glucose was sometimes followed by increased autohaemolysis.

The test for autohaemolysis is clearly useful in the diagnosis of mild cases of hereditary spherocytosis, and also (with the addition of glucose to the blood) in differentiating one type of blood disorder with spherocytosis from another.

J. V. Dacie

MORBID ANATOMY AND CYTOLOGY

1192. The Arnold-Chiari and Other Neuro-anatomical Malformations Associated with Spina Bifida

A. H. CAMERON. *Journal of Pathology and Bacteriology [J. Path. Bact.]* 73, 195-211, 1957. 22 figs., 47 refs.

The morbid anatomy of the Arnold-Chiari malformation and other related malformations is discussed on the basis of the findings in 26 cases of spina bifida seen at necropsy. Features hitherto unrecorded included enlargement of the thalamic massa intermedia, hypoplasia of the falx cerebri, and partial obliteration of the superior longitudinal cerebral fissure. It is suggested that the downward displacement of the medulla and cerebellum and also some of the other changes are the result of altered pressure relations in the amniotic sac and ventricular system of the embryo caused by the escape of the cerebrospinal fluid from the spina bifida.

L. Crome

1193. Malformations of the Neuro-spinal Axis, Urogenital Tract and Foregut in Spina Bifida Attributable to Disturbances of the Blastopore

A. H. CAMERON. *Journal of Pathology and Bacteriology [J. Path. Bact.]* 73, 213-221, 1957. 8 figs., 32 refs.

Twenty-six cases of spina bifida cystica were examined at necropsy; 14 were male and 12 were female, and their ages ranged from 7 hours to 21 months. In one there was a family history of meningocele. There were 12 instances of diastematomyelia. There was severe kyphoscoliosis at the site of the spina bifida in 9 cases, malformations of the ribs and higher vertebrae were present in 5, and malformations of the urogenital tract in 8. There was 1 case with a small cystic spinal teratoma and 1 with a small enteric cyst of the jejunum.

The association between these conditions and spina bifida appears to be due to the fact that all owe their origin to disturbances of the blastopore.—[Author's summary.]

1194. Histochemical Studies on the Cerebral Lipidoses and Other Cellular Metabolic Disorders

B. H. LANDING and D. G. FREIMAN. *American Journal of Pathology [Amer. J. Path.]* 33, 1-12, Jan.-Feb., 1957. 35 refs.

1195. Histochemical Studies of Lymph Nodes in Disseminated Lupus Erythematosus

R. D. MOORE, A. S. WEISBERGER, and E. S. BOWERFIND. *A.M.A. Archives of Pathology [A.M.A. Arch. Path.]* 62, 472-478, Dec., 1956. 6 figs., 27 refs.

Lymph nodes removed at operation or necropsy from 24 patients with disseminated lupus erythematosus were, after appropriate staining, examined by the authors at the Western Reserve University School of Medicine, Cleveland, Ohio, in an attempt to amplify the present concept of the pathogenesis of this disease.

In all these lymph nodes an increase in the number of plasma cells was seen, and some of these cells (usually a few in each section, but occasionally many) contained cytoplasmic inclusions. The inclusions typically were large, eosinophilic masses displacing the nucleus, and gave a positive reaction to periodic-acid-Schiff staining and to the Millon test for protein, and showed pyronophilia which was partly reduced by ribonuclease. It was therefore concluded that they contained carbohydrate, protein, and ribonucleic acid. Similar reactions were given by plasma-cell cytoplasm and by the "haematoxylin bodies", which were present in 9 of the cases examined post mortem. These latter were in addition Feulgen-positive, and were therefore assumed to contain deoxyribonucleic acid. The histological appearances suggested that the haematoxylin bodies were formed by fusion of discharged cytoplasmic inclusions together with some extra-nuclear deoxyribonucleic acid released as the result of necrosis of adjacent cells.

On the basis of these findings the authors advance the theory that the initial change in disseminated lupus erythematosus is the elaboration and release of a protein-carbohydrate complex by the plasma cells, and that the alterations in deoxyribonucleoprotein are secondary.

[There seems to be little in this paper to justify the theory advanced. The histochemical characteristics of plasma-cell cytoplasm here described are certainly not specific for this disease.] *M. C. Berenbaum*

1196. Necrotizing and Healing Pulmonary Arteritis with Advanced Mitral Stenosis

D. M. SPAIN. *A.M.A. Archives of Pathology [A.M.A. Arch. Path.]* 62, 489-493, Dec., 1956. 6 figs., 7 refs.

From the necropsy records of 26 patients dying of rheumatic fever at the Presbyterian Hospital (Columbia University College of Physicians and Surgeons), New York, the author has studied the relationship between rheumatic heart disease and necrotizing pulmonary arteritis. The lesions involved small and medium-sized vessels, especially at bifurcations. Active lesions showed fibrinoid or eosinophilic necrosis, with an intramural and perivascular inflammatory cell infiltrate which included only a few eosinophil granulocytes and no giant cells. Healed lesions were characterized by focal scars, the formation of new vessels in the arterial walls, and intimal fibrosis, the last named sometimes obliterating the arterial lumen; if recanalization occurred the condition resembled healed thrombo-embolism, but could be distinguished from the latter by the presence of focal scarring and the intramural new vessels.

Detailed analysis of these 26 cases revealed no correlation between the activity of the lesion and the activity of the rheumatic state, as judged by clinical or post-mortem findings. The only constant feature was the presence of severe mitral stenosis, and analysis of the records of 600 other cases of rheumatic heart disease showed that necrotizing pulmonary arteritis was never present in the absence of advanced mitral stenosis. The condition was also compared with extrapulmonary arteritis occurring in 15 patients with rheumatic heart disease. In these latter only one or two vessels were involved, whereas many vessels were affected in the pulmonary form, and in all there was active rheumatic fever.

The author concludes that necrotizing pulmonary arteritis is not specifically rheumatic and that, since it is related constantly to advanced mitral stenosis, it is probably due to severe pulmonary hypertension.

M. C. Berenbaum

1197. The Pathology of the Pulmonary Vessels in Hypertensive Disease. (К патологии сосудов легких при гипертонической болезни)

M. A. САМОТЕЙКИН. *Архив Патологии [Arkh. Patol.]* 18, 21-25, No. 7, 1956. 3 figs., 12 refs.

From Saratov State Medical Institute are presented the results of a histological study of the pulmonary blood vessels in 25 fatal cases of hypertensive disease in man and of the pulmonary vessels of 10 rabbits with "reflex hypertension". A general tendency was observed towards hyperplastic changes in the bronchial as well as the pulmonary vessels, and also towards an increase in the number of anastomosing arteries. The bronchial arteries showed the formation of a longitudinal muscle layer internal to the circular muscle layer and hyper-

trophy of the elastic lamina and of the circular muscle layer, with a consequent narrowing of the lumen. In the walls of the pulmonary arteries were noted plaques of atheroma, a uniform intimal thickening with hyperplasia of the elastic lamina, and focal hyaline degeneration. Sclerotic changes were also observed in the walls of the pulmonary veins. Argyrophil fibres of the vascular walls were thickened and coarse. The severity of these changes seemed to depend on the duration of the hypertension rather than on its degree: thus, minimal changes were observed in severe hypertension of recent onset, whereas moderate and even mild elevation of blood pressure over a long period tended to produce severe changes in the pulmonary vessels. The histological findings in rabbits were comparable with those in man.

The cause of these changes in the vessels of the pulmonary circulation in patients with systemic hypertension is said to be found in the functioning of the anastomosing arteries and arterio-venous anastomoses. In the presence of systemic hypertension some blood from the bronchial arteries passes via the anastomosing arteries into the pulmonary arteries, thus raising the pressure in the latter. The same is said to hold true for the veins.

A. Swan

1198. An Investigation into the Lymphatic and Vascular Spread of Carcinoma of the Bronchus

H. C. NOHL. *Thorax [Thorax]* 11, 172-185, Sept., 1956. 13 figs., 22 refs.

A hundred specimens of lungs, resected for bronchogenic carcinoma, have been dissected to determine the site and extent of the growth, and vascular and lymphatic involvement. The findings and conclusions drawn from this investigation are: (1) The incidence of lymph node involvement in the 100 cases was 75%. (2) There is a constant lobar lymphatic drainage, which is described in detail. (3) Lobectomy for bronchogenic carcinoma, where technically feasible, is a sound procedure from the pathological point of view. (4) A comparison of lymphatic invasion rates between the different lobes shows that tumours of the lower lobes on each side have a greater tendency to metastasize than those of the upper lobes, and that if the tumour transgresses the fissure the invasion rate rises significantly.

(5) A surgical-pathological classification, as has been established for cancer at other sites, is proposed. It records the extent of growth, the lymph node infiltration, and the vascular involvement. The purpose of the scheme is to allow comparisons to be made between different forms of treatment, study the different behaviour of the histological types of growths, and assess in future the prognosis of each case. (6) With the aid of this classification the 100 resected cases have been analysed and the following findings ascertained: (a) Of the squamous carcinomata 37.2% showed either no lymphatic involvement or only infiltration of the intrapulmonary nodes, as compared with 17% of the undifferentiated carcinomata. (b) The mediastinal lymph node involvement of the two types was 34% as compared with 60.7% (squamous carcinoma to undifferentiated carcinoma). (c) There was also a difference

in the incidence of vascular involvement—23.7% to 40% (squamous to undifferentiated carcinomata). (d) There was no significant difference between the histological types where the extent of growth was concerned. (e) The peripheral tumours behave in exactly the same way as the central tumours where the extent of the growth and the lymph node involvement are concerned. The vascular infiltration is only slightly more frequent in the central growths, but this may be due to difficulty in demonstrating invasion in the small peripheral vessels, which is thought to occur more frequently, for reasons stated.

(7) The observation that squamous cell carcinomata are more often centrally than peripherally located (66% to 34%) and the adenocarcinomata are in the majority of cases peripheral tumours agrees with the observations by other authors.—[Author's summary.]

1199. A Consideration of Chronic Pulmonary Parenchymal Inflammation and Alveolar Cell Carcinoma with Regard to a Possible Etiologic Relationship

D. L. BEAVER and J. L. SHAPIRO. *American Journal of Medicine* [Amer. J. Med.] **21**, 879–887, Dec., 1956. 7 figs., 46 refs.

In reporting 7 cases of alveolar-cell carcinoma from the Vanderbilt University School of Medicine, Nashville, Tennessee, the authors comment on the increasing frequency of this type of lung cancer. This they suggest may be related to an increasing tendency to post-pneumonic organization and fibrosis. In all their cases chronic non-tuberculous inflammation of the lung of long standing was present, and they consider that the alveolar-cell metaplasia which accompanies it may be a pre-cancerous phase.

G. J. Cunningham

1200. Malignant Tumours of the Thymus Gland. (Злокачественные опухоли вилочковой железы и их распознавание)

B. Y. LUK'YANCHENKO. *Клиническая Медицина* [Klin. Med. (Mosk.)] **34**, 18–22, No. 11, Nov., 1956. 6 figs., 17 refs.

Up to 1940, according to Heuer and Andrus (*Amer. J. Surg.*, 1940, **50**, 146), only 230 cases of mediastinal tumour had been reported in the literature. Taking all types of mediastinal growths and cysts into consideration tumours of the thymus gland (thymomata) constituted 2.1%. These could be divided into three types: (1) carcinoma, 22%; (2) sarcoma (mostly lymphosarcoma), 54.5%; and (3) lympho-epithelioma, 23.5%.

In most cases a malignant thymoma runs a violent course, causing early compression of the organs of the mediastinum, followed by cachexia and rapid death. In the early stages the symptoms are severe pain in the chest, cough, general weakness, and raised temperature. Compression of the large vessels, which occurs very rapidly, leads to oedema of the face, cyanosis, and dilatation of the veins of the chest and hands. Metastases occur very quickly. Usually the radiograph shows a bilateral and symmetrical shadow; as the growth is generally circular in form, resembling a pancake flattened down by the sternum, an antero-posterior radiograph

shows it better than a lateral one. In rare cases the growth may be triangular or oval. Usually the tumour infiltrates only the pleura and the lungs, but sometimes also the sternum. In 3 of the author's cases it spread to the pericardium, myocardium, and aorta. In most cases death ensues within a few months.

H. W. Swann

1201. Transformation of Thyroidal Carcinoma to Clear-cell Type

R. M. KNISELEY and G. A. ANDREWS. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] **26**, 1427–1438, Dec., 1956. 15 figs., 15 refs.

1202. Lipogranulomatous Pseudosarcoid

N. E. WARNER and N. B. FRIEDMAN. *Annals of Internal Medicine* [Ann. intern. Med.] **45**, 662–673, Oct., 1956. 12 figs., 24 refs.

In this study of the incidence of lipogranuloma the authors analysed the findings on examination of 264 spleens obtained at necropsy and 267 gall-bladders removed at operation during the year 1952 at the Cedars of Lebanon Hospital, Los Angeles. Lipogranuloma was present in 17 spleens, an incidence of 6.4%. In 31 of the 267 gall-bladders a lymph node was found adjacent to the cystic duct, and microscopical examination of the lymph nodes showed lipogranuloma in 22, an incidence of 71%. Lipogranulomata in these locations are attributed to absorption of mineral oil from the intestine. The final stage of the lesions, in which there are lipid-laden histiocytes, giant cells, and epithelioid cells, may mimic Boeck's sarcoid, and the term pseudosarcoid is therefore suggested. The lungs, hilar and mesenteric lymph nodes, liver, and bone marrow may also be involved.

The authors discuss the possibility that true sarcoid may also be a lipogranuloma.

E. G. Rees

1203. Some Peculiarities of the Pathological Picture of the Early Stages of Intestinal Amoebiasis. (О некоторых особенностях патологоанатомической картины в ранних стадиях кишечного амёбиоза)

B. ТЕОКХАРОВ. *Архив Патологии* [Ark. Patol.] **18**, 106–109, No. 7, 1956. 3 figs., 8 refs.

Conflicting opinions exist regarding the method of invasion of the intestinal wall by *Entamoeba histolytica*. At the Red Cross Hospital, Sofia, Bulgaria, the author endeavoured to solve the problem by cutting serial sections of the affected portion of the intestine in 6 cases of the disease, so that all stages of the process of invasion of the intestinal wall by the parasite could be observed. From these studies it appears that the amoebae actively penetrate the surface epithelium without inducing any inflammatory reaction. Many of them perish in the depths of the mucosa and there release endotoxins (whose existence has already been established) which cause necrotic changes in the mucosa, thus opening the way for a second wave of invaders. It is these latter which set up the acute inflammatory reaction which constitutes the generally recognized picture of acute amoebic dysentery.

A. Swan

1204. Changes Resembling Periarteritis Nodosa in the Vessels of the Vermiform Appendix. (Изменения в сосудах червеобразного отростка типа узловатого периартериита)

A. S. LEVKINA. *Архив Патологии* [Ark. Patol.] **18**, 76-84, No. 7, 1956. 4 figs., 11 refs.

It is reported from the Second Stalin State Medical Institute, Moscow, that necrotizing arteritis, or rather vasculitis, was found in 35 out of 4,993 appendices removed at operation over a period of 4 years. The annual incidence increased steadily, from 0.36% in 1951 to 0.93% in 1954. The walls of the arteries, and in many cases of the veins also, showed necrosis, fraying of the fibres, necrotic foci, and marked intra- and perivascular leucocytic infiltration. Apart from the vasculitis no other acute inflammatory changes could be detected in these 35 appendices, either macroscopically or microscopically.

The presenting symptom in all cases was pain in the right lower quadrant of the abdomen, simulating either acute or chronic appendicitis. As a rule there was no pyrexia and no leucocytosis. The ratio of females to males was 6:1, and the average age at operation was 30 years. Although in the acute cases, as stated, no other pathological changes were discovered, in the chronic cases submucosal fibrosis, and in long-standing cases complete destruction of the mucosa with stenosis and obliteration of the lumen, were found. The author attributes these sclerotic changes to ischaemia, and the pain (in an otherwise symptomless course of vasculitis) to vascular spasm. The probability of the vasculitis being of an allergic nature is considered and the possible role of sulphonamides and penicillin briefly discussed.

A. Swan

1205. Distal Tubular and Proximal Tubular Necrosis in the Kidneys of Burned Patients

S. SEVITT. *Journal of Clinical Pathology* [J. clin. Path.] **9**, 279-294, Nov., 1956. 11 figs., 25 refs.

A report is presented of the results of histological examination of the kidneys of 86 fatally burned patients admitted to the Accident Hospital (M.R.C. Burns Research Unit), Birmingham. Acute proximal tubular necrosis was observed in 17 of these cases and acute distal tubular necrosis in 34. Proximal tubular necrosis occurs mainly in elderly subjects who have nephrosclerosis, and is usually associated with severe oliguria, whereas distal necrosis mainly affects children and younger adults and may or may not be associated with acute renal failure. Diffuse distal necrosis, which affects many nephrons and corresponds to Lucké's lower nephron nephrosis, was found in 16 patients and was associated with anuria or severe oliguria, or alternatively with a non-oliguric form of acute uraemia. Focal distal necrosis, affecting only a few nephrons, occurred in 18 patients, most of whom were children; it was seldom associated with acute renal failure and was rarely of clinical importance.

Details, some of which are illustrated in photomicrographs, are given of the gross and histological appearances of the kidneys. It is pointed out that proximal

and distal tubular necrosis are histologically distinct, although in a few cases there was evidence of the presence of both lesions. The pathogenesis of these conditions is discussed. In the author's opinion the main body of evidence indicates that the proximal tubular necrosis occurring after burning is produced by renal ischaemia of vasomotor origin. It has been suggested that haem compounds may be of aetiological significance in the development of diffuse distal tubular necrosis, but since haemoglobin itself is thought to be non-toxic, other factors must also be present to account for the necrosis. Oligaemia producing renal vasoconstriction and ischaemia may be responsible, and this hypothesis is under investigation.

A. W. H. Foxell

1206. Dissimilarity of Retinal Micro-aneurysm and Glomerular Nodule in Diabetes

D. VOLK. *A.M.A. Archives of Ophthalmology* [A.M.A. Arch. Ophthal.] **56**, 188-193, Aug., 1956. 4 figs., 3 refs.

It is suggested that the differences between the specific retinal lesions and the renal lesions in diabetes mellitus, particularly in regard to time of onset, mode of development, relative prevalence, and histological appearances, indicate that there are basic differences in the pathogenesis of the two types of lesion. Thus the retinal lesion (micro-aneurysm) appears early in the course of the disease, is not necessarily associated with hypertension, and does not usually indicate a bad prognosis. The renal lesion (intercapillary glomerulosclerosis), on the other hand, appears later, is associated with hypertension and albuminuria, and carries a bad prognosis for the life of the patient. Only as the retinopathy becomes more severe does the nephropathy make its appearance, and the latter is never seen without the former. When the renal lesions develop the diabetic retinopathy may be complicated by the occurrence of retinopathy of renal origin.

Histologically, the renal lesion is not a micro-aneurysm but consists of a hyalinized nodule which develops as the result of progressive proliferation of connective tissue around normal-sized or dilated glomerular capillaries. It is composed of circumferentially laminated, finely fibrillated hyalin, and contains some cells within and one or more layers of cells at the periphery. A layer of capillaries surrounds the nodule and one or more capillaries may be seen within the nodule. It stains positively for connective tissue, and other staining reactions suggest it has a high mucopolysaccharide content. The retinal lesion is based on a micro-aneurysm which later develops a thickened wall of laminated structure, described by Ashton as exudate; this also has a high mucopolysaccharide content, but no cells or connective tissue are present. Histologically, therefore, these lesions are similar in one respect only, namely, their high mucopolysaccharide content.

C. G. Tulloh

1207. Tissue Culture as a Possible Aid in Recognizing the Origin of Cystic Hygroma

J. GRIEVE and J. D. B. MACDOUGALL. *Archives of Disease in Childhood* [Arch. Dis. Childh.] **32**, 35-37, Feb., 1957. 5 figs., 4 refs.

Microbiology and Parasitology

1208. Cultivation of *M. tuberculosis* from Urine and Gastric Lavage by the Pancreatin-Quaternary Ammonium Compound Method

R. SAXHOLM. *American Review of Tuberculosis and Pulmonary Diseases* [Amer. Rev. Tuberc.] 74, 616-621, Oct., 1956. 4 refs.

In a previous paper (*Amer. Rev. Tuberc.*, 1955, 72, 98) the author described the use of pancreatin and methylphenyldodecyltrimethylammonium methosulphate ("desogen") for culture of tubercle bacilli from sputum specimens. In the present paper from the State Institute of Public Health, Oslo, he reports the application of this method to urine and gastric washings. Whole urine or the sediment from centrifuged gastric washings was mixed with pancreatin and desogen, the mixture being kept in stoppered tubes in the dark for 24 hours at room temperature. The urine was centrifuged and the sediment inoculated on to Löwenstein-Jensen slants. The mixture from gastric lavage was not centrifuged and was inoculated direct. In some experiments urine and specimens of gastric washings were treated with 4% sodium hydroxide and the number of positive cultures of tubercle bacilli compared with that obtained by the pancreatin-quaternary ammonium compound method. The latter compared favourably with the sodium hydroxide method; technically, it was not more difficult to perform, and the number of cultures contaminated by organisms other than mycobacteria was approximately the same.

R. Hare

1209. Cervical Lymphadenitis in Children Caused by Chromogenic Mycobacteria

F. H. PRISSICK and A. M. MASSON. *Canadian Medical Association Journal* [Canad. med. Ass. J.] 75, 798-803, Nov. 15, 1956. 41 refs.

In this paper from McGill University and the Children's Hospital, Montreal, an account is given of 10 cases of cervical, facial, or submaxillary lymphadenitis in young children in which the clinical picture resembled tuberculous infection, and pus from lymph nodes yielded on culture a chromogenic acid-fast and alcohol-fast bacillus. In addition 2 cases of empyema in adults and 2 of other lesions in children in which a similar organism was isolated are described.

The clinical course of the cervical and facial lesions was comparatively benign, the lesions healing slowly without sinus formation. The histological picture of resected lymph nodes was indistinguishable from that seen in tuberculosis. Bacteriological examination showed that the characteristics of the organism were more nearly those of mycobacteria usually pathogenic to man and animals than of saprophytic varieties. The organism grew slowly at room temperature, and produced a pigment varying from yellow to deep orange. In inoculation experiments in guinea-pigs and rats local lesions were frequently observed at the site of injection; only

one of a number of hens showed generalized disease. The results of Mantoux tests with human and avian tuberculin were negative except that in most of the hens there was a positive reaction to avian old tuberculin (O.T.). In all except one of the animals a positive result was obtained with tuberculin derived from the corresponding chromogenic strain.

The authors do not consider that these mycobacteria are chromogenic variants of human, bovine, or avian tubercle bacilli because of the lack of response to the appropriate variety of O.T.; neither do they consider that they are saprophytes or contaminants. They propose the name *Mycobacterium scrofulaceum* (nov. sp.) for this organism.

John M. Talbot

1210. Retention and Differentiation of Mycobacteria in Tissue Sections

J. H. HANKS. *American Review of Tuberculosis and Pulmonary Diseases* [Amer. Rev. Tuberc.] 74, 608-615, Oct., 1956. 8 refs.

1211. The Use of Mice in the Bacteriological Diagnosis of Tuberculosis. Application to the Rapid Determination of Drug Sensitivity. (Utilisation de la souris pour le diagnostic bactériologique de la tuberculose. Application à l'étude rapide de la sensibilité aux médicaments) H. NOUFLARD and S. BERTEAUX. *Revue française d'études cliniques et biologiques* [Rev. franç. Ét. clin. biol.] 1, 869-876, Oct., 1956. 1 fig., 7 refs.

The authors, working at the Hôpital Léon-Bernard, Brévannes, Seine-et-Oise, have developed a new and rapid method for the isolation of tubercle bacilli and the determination of their sensitivity to antituberculous agents. The method is based on the techniques of slide-culture of sputum devised some years ago which unfortunately, however, were applicable only to specimens of sputum containing abundant organisms. The authors' method consists in the intravenous injection of various pathological materials into mice and the subsequent culture of smears from the spleen of these animals by a slide-culture technique.

The material injected included cerebrospinal fluid and gastric aspirate; after centrifugation the sediment was resuspended in 2 ml. of Dubos medium containing bovine albumin (Fraction V) but no "tween 80", or alternatively in a 0.5% solution of bovine albumin Fraction V in water. Specimens of urine and exudates from the body cavities were injected untreated; pus was diluted in a 0.5% solution of bovine albumin until sufficiently fluid for injection, and tissues were ground up and suspended also in the albumin solution. About 0.25 ml. of one of these preparations was injected into the tail vein of young white mice aged 3 to 4 weeks. It was noted that treatment of the mice with cortisone (20 mg. per kg. body weight per day) seemed to increase

the number of positive results. The animals were divided into three groups and killed 8, 15, and 21 days respectively after injection, when the spleens were removed and ground up aseptically with 1 ml. of liquid Dubos medium or bovine albumin. Smears from each spleen suspension were made on about a dozen narrow glass slides, half the width of the glass slide commonly used. The slides were dried in sterile Petri dishes, immersed in 6% sulphuric acid for 6 minutes, and then in sterile water in another Petri dish. The parts of the slide covered with spleen smear were then immersed in Dubos medium without tween 80 but containing the antibiotic being tested for resistance. The slide cultures were incubated for 6 to 10 days, after which one of the control slides was taken out and stained for tubercle bacilli. If 20 colonies per slide were seen under the low power of the microscope then the other slides which had been cultured with antibiotics were also removed and stained.

Out of 43 specimens of materials tested, 7 positive results were obtained, 5 with cerebrospinal fluid. The authors found the mouse-spleen method of isolation to have an efficiency comparable to that of Löwenstein-Jensen medium, and sensitivity tests in Dubos medium gave results similar to their slide-culture method. In artificial mixtures of sensitive and resistant strains of tubercle bacilli the resistant organisms could be detected if present in a concentration of 1% or more. The mean time required for the determination of sensitivity of tubercle bacilli to antituberculous agents was 26.4 days from the receipt of the original specimen, compared with a mean (100 tests) of 67.4 days by the usual method. The authors agree that their method is not suitable for routine use, but suggest that it may be useful in selected cases in which a quick result is particularly desired.

B. Ruebner

1212. **The Distribution of Phage Types of Typhoid Bacillus in the Soviet Union.** (Распространенность фаготипов брюшнотифозного микроба в СССР) R. I. ZUBKOVA. *Журнал Микробиологии, Эпидемиологии и Иммунологии* [Zh. Mikrobiol.] 69-74, No. 11, Nov., 1956.

A total of 1,121 strains of *Salmonella typhosa* isolated in all parts of Russia were examined at the Gamaleya Institute of Epidemiology and Microbiology. Twelve different phage types—A, B2, C, D, D2, D4, D5, D6, E, F, M, and T—were identified, Types F, A, and E making up 84.8% of the strains typed. Only 3.8% of the strains were imperfect and untypable. There was a considerable uniformity of types in the over-all picture; this was particularly marked in strains from the outlying parts of Russia, whereas in those from the central parts there was greater variety. No great fluctuation of types occurred during the period of observation (1944-51). Capacity to ferment xylose seemed to be of some interest as regards differentiation, as 70% of strains gave a positive and 30% a negative reaction, while 99.2% fermented arabinose. However, no relationship could be established between the fermentation reactions or content of Vi antigen on the one hand and phage type on the

other, nor was there any association between phage type and clinical severity of the illness caused.

In conclusion it is stated that the uniform picture of phage-type distribution suggests the practicability of prophylactic measures applicable to the whole of Russia and consisting of a typhoid phage preparation composed of the three most frequent phage types of the typhoid bacillus.

K. Zinnemann

SEROLOGY AND IMMUNOLOGY

1213. **Cysticercosis of the Nervous System. Diagnosis by Means of the Spinal Fluid Complement Fixation Test** D. NIETO. *Neurology* [Neurology] 6, 725-738, Oct., 1956. 8 figs., 21 refs.

Writing from the Institute of Medical and Biological Studies of the National University of Mexico the author discusses the clinical pathology and diagnosis of cysticercosis of the central nervous system (C.N.S.), which is relatively common in the population of Mexico. He states that the presenting clinical signs and symptoms are so varied that a diagnosis on clinical grounds alone is practically impossible. In the 168 cases here reviewed the most frequent symptoms were: (1) generalized epilepsy, (2) intracranial hypertension similar to that due to cerebral tumour, and (3) basal meningitis, in which mental symptoms predominated. The author emphasizes that many cases present psychic disturbance only. The pathological changes, both macroscopic and microscopic, are also very varied, a great variety of lesions being present, although inflammation is the most constant. But the areas of the brain affected vary greatly, and even in histological preparations it may be impossible to locate the parasite or, if it has been present in the brain for many years, to identify it, since its structure has usually completely degenerated. However, the cerebrospinal fluid (C.S.F.) in some cases shows characteristic changes, such as an increase in the number of cells, sometimes with an eosinophilia, and a decrease in the glucose and a variable increase in the protein content; the globulin reaction is usually positive.

Because of the difficulty of diagnosis the author has attempted to evolve a complement-fixation test for *Cysticercus*. The antigen was prepared from *Cysticercus* cysts, collected from highly infected pork and freed from all connective tissue, by drying an extract of the clean cysts in alcohol. With this extract as antigen a complement-fixation test similar to the Wassermann reaction was performed. Control tests on the blood of infected pigs were always strongly positive and tests on a series of 40 samples of normal spinal fluid were completely negative. By means of this complement-fixation test it has been possible to identify 168 cases of cysticercosis of the C.N.S. in the last 12 years, the diagnosis being confirmed at necropsy in 18 cases and at operation in 40. Although there was no absolute proof in the remaining cases the clinical findings were compatible with such a diagnosis. The reaction has also been employed to test serum from patients with a number of other diseases of the C.N.S., but with consistently negative results except in cases of neurosyphilis; thus some 30% of samples

of C.S.F. giving a positive Wassermann reaction also gave a positive *Cysticercus* reaction. Although it is possible that these patients had a double infection the author considers that the positive cysticercosis reactions were probably false reactions, and suggests that diagnosis may be helped by using a weaker antigen. The reaction with fluid from the ventricles was often much weaker than that with lumbar C.S.F., but cisternal fluid always gave results similar to lumbar fluid.

It has not been possible to determine at what stage in the disease the reaction becomes positive, most of the author's cases being of several years' duration, but in one patient with subcutaneous cysticercosis of 2 months' duration the reaction was negative. The test has also been performed as a routine on over 12,000 samples of blood serum in the same period; the blood serum of 15% of the population of a psychiatric hospital gave a positive reaction. Most of these reactions were not cross-reactions with other serological tests, although there was some suggestion that a positive Wassermann reaction gave a false cysticercosis reaction. Of 148 cases of cysticercosis tested, the blood serum gave a positive reaction in 66, but in 7 cases of the disease confirmed at necropsy the blood reaction had been negative.

R. F. Jennison

1214. An Improved Technique for the Neutralization Test with Adenoviruses in HeLa Cell Cultures

J. T. GRAYSTON, P. B. JOHNSTON, M. E. SMITH, and C. G. LOOSLI. *Journal of Infectious Diseases* [*J. infect. Dis.*] 99, 188-198, Sept.-Oct., 1956. 2 figs., 12 refs.

A simplified neutralization test for adenoviruses is described in this paper from the University of Chicago School of Medicine, in which the main difference from the usual test is that the serum and virus are added to the culture tubes at the same time as the HeLa cells, the tubes being then immediately slanted and incubated at 37° C. Further simplification was gained by using HeLa cells grown in a medium with horse serum rather than human serum, thus avoiding the necessity of washing the cells before use.

Stock adenoviruses of Types 1 to 10 were individually diluted so that the virus antigen of each type was that amount without excess which produced Grade-4 "cytopathogenesis" in HeLa cells under the conditions of the test. Serum dilutions of from 1 in 2 to 1 in 512 were tested. Each tube of the test contained 1.0 ml., that is, 0.1 ml. of diluted serum, 0.2 ml. of virus antigen, and 100,000 HeLa cells in 0.7 ml. of Eagle's medium containing 10% horse serum. After incubation for 48 hours the tubes were examined under low-power magnification for degree of pathological change in the cells, which was assessed as *nil* or Grades 1 to 4. The end-point was taken as the greatest serum dilution allowing normal growth of HeLa cells and a degree of cytopathogenesis not greater than Grade 1. Samples of rabbit type-specific antiserum and paired samples of human serum from patients with acute adenovirus respiratory infection were subjected to the test. The authors found the "break-through" of the neutralizing effect of the sera by the virus was minimal, the grades of cytopathogenesis

at 24 and 48 hours of incubation being in fact usually the same. This simplified procedure gave consistent and repeatable results, and the serum titres obtained were similar to those found with the conventional method.

Joyce Wright

1215. Neutralizing and Complement Fixing Antibody Response to Adenovirus Infection

J. T. GRAYSTON, C. G. LOOSLI, P. B. JOHNSTON, M. E. SMITH, and R. L. WOOLRIDGE. *Journal of Infectious Diseases* [*J. infect. Dis.*] 99, 199-206, Sept.-Oct., 1956. 14 refs.

The neutralizing and complement-fixing antibody response to adenovirus antigens is reported for 53 patients suffering acute respiratory illnesses and having an adenovirus, either Type 3, 4, or 7, isolated from their upper respiratory tracts. A complement-fixing antibody titer rise of fourfold or greater between the acute and convalescent serum samples was demonstrated for each of the patients. Fifty-one of the patients had fourfold rises in neutralizing antibody against the isolated virus prototype. The two patients failing to show a rise in neutralizing antibodies had present in their acute serum samples neutralizing antibody against the virus type isolated. In addition to neutralizing antibody rises against the homotypic virus antigen, tests with adenovirus Types 1 through 10 showed heterotypic rises with each antigen type in from 13 to 44% of the serum pairs. Neutralizing antibodies were found in the acute serum samples frequently with antigen Types 1, 2, 3, 5, and 6, infrequently with Types 4, 7, 8, and 10, and not at all with Type 9. No relationship between the presence of antibody in the acute serum and the occurrence of a heterotypic neutralization antibody rise could be demonstrated.—[Authors' summary.]

1216. Vaccination Against Poliomyelitis with Live Virus Vaccines. 1. A Trial of TN Type II Vaccine. 2. A Trial of SM Type I Attenuated Poliomyelitis Virus Vaccine. 3. The Evaluation of TN and SM Virus Vaccines

D. S. DANE, J. H. CONNOLLY, G. W. A. DICK, O. D. FISHER, and F. McKEOWN. *British Medical Journal* [*Brit. med. J.*] 1, 59-74, Jan. 12, 1957. 7 figs., 16 refs.

In the first part of an investigation carried out at the Queen's University of Belfast, the oral administration of 500,000 MPD₅₀ (the dose causing paralysis in 50% of cases on administration to mice) of the mouse-adapted non-cytopathogenic TN Type II poliovirus vaccine in milk to 21 adult volunteers, 10 infants, and 159 children resulted in the development of Type-II antibody in 4 (22%) of the 18 adults and in 96 (77%) of the 124 children whose blood contained no Type-II antibody at the time of vaccination. The geometric mean antibody titre in the 96 children was 1 in 66. Siblings responded in a similar way in 22 out of 24 pairs. Amongst the infants, 6 had moderate levels of passively acquired Type-II antibody at some time before vaccination. Three of these whose blood still contained a moderate titre at the time of vaccination developed active immunity and 5 infants in all developed levels greater than 1 in 16. The infants and children who developed antibody

excreted virus in their faeces in titres as high as $10^{6.4}$ TCD₅₀ and in some cases for more than 4 weeks. This TN faecal virus, unlike the TN vaccine virus, was cytopathogenic in monkey kidney tissue cultures and caused severe paralysis when inoculated intracerebrally into monkeys. No serious illness developed within a month of vaccination in any of the subjects, but minor illnesses were reported in 13 of 73 children who developed antibody compared with 3 of 34 children who had no response. This difference is not significant.

In the second part of the investigation the oral administration of 2,500 TCD₅₀ of the SM Type-I attenuated poliovirus vaccine in capsules to 11 adults and of 6,400 TCD₅₀ in milk to 2 infants with moderate titres of maternally acquired Type-I antibody and one child in a family with susceptible members resulted in all cases in the development of active immunity. During the months following vaccination a decline in circulating antibody from the highest peak reached was observed in most of the adults. All the subjects became faecal carriers of the virus for one to more than 7 weeks, and high titres of virus were found in early specimens of faeces from some individuals. No virus was isolated from the throat. One adult who, unlike the others, had had no Type-II antibody in his blood before vaccination, had a trace amount of virus in his blood on the 8th day and developed the highest Type-I antibody titre and a low Type-II antibody titre. Although no evidence of transmission of the virus from the adults was found, the mother and younger brother, but not the older sister, of the vaccinated child became infected and developed Type-I antibody. The brother became a faecal carrier 5 days after his sister had received the vaccine. The SM faecal virus, unlike the SM vaccine virus, caused paralysis in some monkeys when injected intracerebrally. No serious illness occurred in any of the 16 subjects, but minor illnesses occurred within a month of vaccination in 9.

Discussing these findings in the third part of this paper, Dick and Dane point out that the difference in response of adults and children to infection with these attenuated poliovirus vaccines suggests that in certain population groups some adults may develop barriers other than homotypic circulating antibody to infection with some strains of poliovirus, while some families may be genetically relatively more resistant to infection than others. The results of these trials differ from those reported by Koprowski *et al.* (*J. Amer. med. Ass.*, 1956, **160**, 954; *Abstracts of World Medicine*, 1956, **20**, 256) in that the titre of circulating Type-I antibody declined in the adults tested in the months following vaccination, the TN virus was excreted in high titre and for a considerable period, and that the TN and SM faecal viruses differed markedly in character from the vaccine viruses and did not seem to differ in any measurable way from naturally occurring strains. The proportion of individuals developing antibody after receiving the TN vaccine was less than with Salk-type vaccine, but this could have been due to the relative insusceptibility of certain individuals to infection. All these vaccinations were performed outside the poliomyelitis season, and it is not known how attenuated virus might behave at other times

of the year. It is considered that these vaccines are not at the moment acceptable for mass immunization. The minimum requirements for attenuated poliovirus vaccines are outlined.

A. Ackroyd

1217. **A Method of Determining the Toxigenicity of Diphtheria Bacilli *in vitro* and the Possibility of Its Application. I. Determination of Toxigenicity of Pure and Mixed Cultures of Diphtheria Bacilli.** (Метод определения токсигенности дифтерийных микробов *in vitro* и перспективы его применения. Сообщение 1. Определение токсигенности чистых и смешанных культур дифтерийной палочки)

N. I. VOLOVICH and M. M. LEIKINA. *Журнал Микробиологии, Эпидемиологии и Иммунологии* [Zh. Mikrobiol.] 30-34, No. 12, Dec., 1956. 13 refs.

Elek's agar diffusion technique for the demonstration *in vitro* of the toxigenicity of strains of *Corynebacterium diphtheriae* (*Brit. med. J.*, 1948, **1**, 493; *Abstracts of World Medicine*, 1948, **4**, 156) has been reinvestigated at the Metchnikov Institute for Vaccines and Sera, Kharkov, with a view to its routine application as a virulence test in clinical laboratories. It was realised that the production of toxin by strains under investigation depends largely on the use of a culture medium which favours such toxin production. For this reason 0.003% of cystine was added to Elek's medium as modified by Frobisher *et al.* (*Amer. J. clin. Path.*, 1951, **25**, 282), which contains 50% less maltose and 5 times more lactic acid than the medium originally described.

In intracutaneous virulence tests on guinea-pigs 67 strains were found to be toxigenic and 36 non-toxigenic. All strains which were toxigenic *in vivo* proved also to be toxigenic *in vitro* after 48 hours' incubation. Eight of the strains which were non-toxigenic *in vivo* were, however, toxigenic *in vitro* after 48 hours' incubation, but when these strains were tested again *in vivo* by injecting a much larger dose—2,000 million organisms—subcutaneously all 8 proved to be toxigenic. These findings appear to prove the superiority of Elek's technique over the intracutaneous test for toxigenicity.

It was considered that the isolation of pure diphtheria strains would complicate unnecessarily the work of the laboratory and for this reason mixed cultures were tested in the same way. It had been established previously that as few as 5 to 50 diphtheria bacilli per ml., when inoculated on to Elek plates, gave rise to well-marked precipitation lines; furthermore, that 90% of carriers of virulent diphtheria strains yield no less, and in many cases far more, than 1,000 diphtheria bacilli per throat swab. A total of 146 mixed cultures from Loeffler slopes were inoculated on to Elek plates, 45 of which had proved to be toxigenic and 101 non-toxigenic in tests on guinea-pigs. *In vitro* 42 were toxigenic after 48 hours, while the results with non-toxigenic strains were identical with those obtained *in vivo*.

The authors suggest that the determination of toxigenicity of diphtheria strains is feasible in mixed cultures and could serve as a routine technique. They go even farther and suggest that the method might be exploited for the bacteriological diagnosis of clinical diphtheria.

K. Zimmernann

Pharmacology

1218. Clinical Trial of Methypylone, a Piperidine Hypnotic

J. S. STEWART. *British Medical Journal* [Brit. med. J.] 2, 1465-1467, Dec. 22, 1956. 5 refs.

A controlled clinical trial of the new hypnotic drug methypylone ("noludar") was carried out on 100 patients aged 21 to 71 years in the ear, nose, and throat wards of the Middlesex Hospital, London. Four indistinguishable tablets were used, containing respectively 100 mg. of amylobarbitone sodium, 100 mg. of butobarbitone, 200 mg. of methypylone, and an inert material, and the patients received each of these in turn during the first four nights in hospital, excluding the night after operation. The order in which the drugs were given varied and was unknown to the patients and staff. Every half-hour between 10 p.m. and 6 a.m. the night nurse recorded whether the patients were sound asleep, dozing lightly, or awake, and awarded a score each half-hour of 2, 1, or 0 respectively. The total score for the night was taken as a measure of the average depth and duration of sleep.

The trial revealed no difference between the three drugs in hypnotic effect, but all three differed significantly, although not strikingly, from the inert material. Subjective evaluation of the drugs was made by asking the patients next morning about the onset and quality of sleep and the occurrence of after-effects. More rapid onset and deeper sleep was recorded for each of the three drugs than for the control material, but no difference was detected between the drugs. There was no significant difference between the drugs and the control material in regard to occurrence of after-effects; about one-quarter of the patients complained of feeling "stale and drowsy" in the morning after each of the four tablets.

It was concluded from the trial that methypylone is a reliable hypnotic, comparable with amylobarbitone sodium and butobarbitone in efficacy and onset and duration of action.

Bernard Isaacs

1219. The Influence of Reserpine on the Endocrine Glands. (Influence de la réserpine sur les glandes endocrines)

H. TUCHMANN-DUPLESSIS. *Presse médicale* [Presse méd.] 64, 2189-2192, Dec. 25, 1956. 15 figs., 27 refs.

The author reports that studies of the effect of reserpine on the endocrine system, carried out at the laboratories of the Faculté de Médecine, Paris, have shown that the administration of reserpine to rats produces undesirable effects on many of the endocrine glands. Adult rats were given daily doses of reserpine (0.25 mg. per kg. body weight intramuscularly) for 15 to 35 days, some groups of female animals also receiving oestradiol (3 to 10 µg. per kg.), while some groups of males received testosterone (0.25 to 1 mg. per kg.). In the female rats

there was hypofunction of the genital system, which resulted in regression of the ovary and suppression of oestrus. This action appeared to be reversible, however, since 6 to 8 days after cessation of treatment with reserpine the oestrous cycle returned to normal. In the male rats spermatogenesis was maintained, but the testicular interstitial tissue atrophied. There was also atrophy of the epithelium of the prostate and of the seminal vesicles.

Histological examination showed that the activity of the thyroid gland was often diminished, whereas that of the adrenal cortex was increased. It is concluded from these findings that reserpine may be of value in treating patients exhibiting certain hypersecretions of the genital system.

[No suggestions regarding the possible mechanism of action of reserpine are offered.]

G. B. West

1220. Studies on the Neutralizing Effect and Antipeptic Properties of Some Commonly Used Antacids. [In English]

P. KOSKINEN. *Annales medicinae internae Fenniae* [Ann. Med. intern. Fenn.] 45, Suppl. 25, 1-90, 1956. 25 figs., bibliography.

1221. Quantitative Comparison of Cough-suppressing Effects of Romilar and Other Antitussives

L. J. CASS and W. S. FREDERIK. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 48, 879-885, Dec., 1956. 3 figs., 4 refs.

A comparative clinical study of the efficacy of certain cough suppressants, notably dextromethorphan hydrobromide ("romilar") and codeine sulphate, is reported from Harvard University and School of Public Health, Boston. Some 63 patients with chronic cough were given a 10-day course of each of the following: 10 mg. of dextromethorphan, 20 mg. of dextromethorphan, 15 mg. of codeine sulphate, and 10 mg. of caramiphen ethanedisulphonate ("taoryl"); between the courses, given in a random sequence, they received a placebo for 3 days, the drugs and placebo being supplied in tablets of identical appearance. One tablet was taken 4 times a day, and the degree of cough recorded 3 times a day by an observer who was unaware of the nature of the medication.

It was found that dextromethorphan at both dose levels and a dose of 15 mg. of codeine sulphate had approximately the same cough-suppressant activity; caramiphen was less effective and the placebo had no significant action.

T. B. Begg

1222. Utilization and Toxicity of Peptonized Iron and Ferrous Sulfate

J. H. KEITH. *American Journal of Clinical Nutrition* [Amer. J. clin. Nutr.] 5, 35-38, Jan.-Feb., 1957. 7 refs.

Chemotherapy

1223. Antibiotic and Cytostatic Properties of the Actinomycins

L. H. PUGH, E. KATZ, and S. A. WAKSMAN. *Journal of Bacteriology* [J. Bact.] 72, 660-665, Nov., 1956. 1 fig., 11 refs.

A number of homogeneous components have recently been separated from the various actinomycins isolated from members of the *Streptomyces* species. The effect of these substances on various species of bacteria, mycobacteria, yeasts, and fungi, and on two experimental mouse tumours has been studied at Rutgers University, New Brunswick, New Jersey.

Actinomycins A, B, C, and D were found to have similar activity, but the various pure fractions isolated from them did not always possess comparable potency. The effect of actinomycins C and D and certain other crystalline components on experimental Gardner's lymphosarcoma in the ascitic form, and on transplantable mammary lymphosarcoma in mice, did not parallel the results obtained in the microbiological systems. The assessment of toxicity, using the mouse spleen weight method, also failed to indicate anti-tumour activity. Actinomycin C inhibited the growth of adenocarcinoma during the period of its administration. Certain of the pure fractions also exhibited some anti-tumour properties, 80% of mice with the lymphosarcoma surviving for over 2 months compared with a control time of 12-8 days.

These results are taken to indicate that a useful chemotherapeutic agent against cancer may eventually be isolated from one or other of the actinomycetes.

Kenneth Gurling

1224. Some Laboratory and Clinical Experiences with a New Antibiotic, Vancomycin

J. E. GERACI, F. R. HEILMAN, D. R. NICHOLS, W. E. WELLMAN, and G. T. ROSS. *Proceedings of the Staff Meetings of the Mayo Clinic* [Proc. Mayo Clin.] 31, 564-582, Oct. 17, 1956. 3 refs.

The authors report from the Mayo Clinic some laboratory and clinical experiences with vancomycin, a new antibiotic obtained from *Streptomyces orientalis*. In studies of the bacteriostatic effect of the antibiotic on various organisms it was found that 95 out of 112 strains of *Staphylococcus aureus* were inhibited by a concentration of 2.5 $\mu\text{g. per ml.}$, 15 by 1.25 $\mu\text{g. per ml.}$, and 2 by 5 $\mu\text{g. per ml.}$ These tests were carried out with serial dilutions of the antibiotic in plates of nutrient agar. It was found that there was some variation in the sensitivity according to the method of assay. Of 28 strains of *Streptococcus faecalis*, 16 required 2.5 $\mu\text{g. per ml.}$ for inhibition, 11 required 5 $\mu\text{g.}$, and one strain 12 $\mu\text{g. per ml.}$ A number of strains of *Clostridium* were also tested in thioglycolate broth; in this the inhibitory

concentration varied from 0.39 to 5 $\mu\text{g. per ml.}$ and the bactericidal concentration from 0.78 to more than 10 $\mu\text{g. per ml.}$

Some further experiments showed that vancomycin is bactericidal as well as bacteriostatic and that the concentration required for total inhibition of growth was the same or nearly the same as the bactericidal concentration, at least in the case of *Staph. aureus*. It was also evident that the activity of vancomycin was not greatly affected by the presence of serum.

The drug was also tested against 12 strains of *Strep. mitis* isolated from the blood of patients with subacute bacterial endocarditis. These organisms showed a wide variation of sensitivity, especially as to the bactericidal concentration, which varied from 0.312 $\mu\text{g.}$ to more than 10 $\mu\text{g. per ml.}$ It was possible to make strains of *Staph. aureus* resistant to vancomycin by continuous subculturing in media containing the antibiotic, but this effect was slow to appear. The drug was found to have a good protective effect when given to animals before experimental infection with *Staph. aureus*. The antibiotic had no effect, however, in experimental infection of mice with *Toxoplasma gondii*.

Examination of the faeces of 14 patients receiving vancomycin showed that while the Gram-negative flora persisted, Gram-positive organisms were reduced in number or disappeared. The concentration of vancomycin appearing in various body fluids was then determined, using an agar-diffusion method. This showed that little or no vancomycin appeared in the blood serum and only small amounts in the urine after oral administration of 400 mg. every 6 hours. In 8 healthy young men a single intravenous injection of 500 mg. produced a mean serum concentration of 33 $\mu\text{g. per ml.}$ at one minute, and this decreased only gradually so that after 24 hours the value was still 0.7 $\mu\text{g. per ml.}$ Following intravenous administration large quantities of the antibiotic were excreted in the urine, and at the end of 24 hours the urinary concentration was still 100 $\mu\text{g. per ml.}$, suggesting that it is excreted chiefly through the kidneys. After single or multiple intravenous injections of vancomycin adequate therapeutic levels were found in the pleural, pericardial, ascitic, and synovial fluids. These tests were carried out on patients with non-inflammatory lesions of these body cavities who were having fluid removed for other purposes. A few patients were given vancomycin before undergoing cholecystectomy, but only small amounts of the drug appeared in the bile. It was noted that after intravenous injection the amount of drug in the stool was considerably less than after oral administration. Vancomycin did not appear to diffuse through the uninflamed meninges.

The only signs of toxicity encountered were an occasional "chill", presumably due to pyrogens or other impurities, this being noted in only 6 out of

94 patients. A skin reaction occurred in 4 cases, and phlebitis had occurred following injections in some of the patients treated earlier; also some local discomfort occurred if the injection leaked around the veins. Short case histories of 9 patients treated with vancomycin are presented.

R. F. Jennison

1225. Advanced Cancer Treated with Nitromin

B. A. STOLL. *Medical Journal of Australia* [Med. J. Aust.] 2, 882-887, Dec. 15, 1956. 3 figs., 13 refs.

Nitrogen mustard (methyl bis-(β -chloroethyl)-amine hydrochloride) and certain other derivatives of mustard gas have been used with occasional success in the treatment of cancer and the reticuloses. "Nitromin", introduced clinically by Japanese workers in 1949, is nitrogen mustard-N-oxide and is of special interest because the ratio between the maximum tolerated dose and the minimum effective dose for rat ascites sarcoma is four times higher than that of nitrogen mustard itself. The compound has been used in a variety of conditions, but most reports suggest that it produces only temporary inhibition of the tumour growth, followed by recurrence; the growth may respond a second time, but death occurs from further manifestations of the disease. Histologically, treatment results in necrosis and degeneration of the tumour cells. Unlike nitrogen mustard, nitromin has no vesicant action on the skin or mucous membranes provided it is well diluted. Its action on the blood cells is slower, and recovery is more rapid. Nausea and vomiting may occur after the first dose, but usually disappear later or can be abolished by dividing the daily dose in two, while generally resistance to the compound does not develop with a second course. Whether nitromin is given intravenously or orally, the recommended dose is 1 mg. per kg. body weight, 50 mg. being dissolved in 50 ml. of saline for injection or oral administration. By mouth it should be given 3 hours after a meal or before retiring at night. A full course generally consists of 750 mg. given in 15 to 20 days, response to this treatment usually being apparent after the first week.

Alkylating agents such as nitrogen mustard and nitromin combine readily with nucleic acids, purines, and pyrimidines, and experiments *in vivo* have shown that they become fixed to these chemicals in the nuclei of cells, causing chromosomal aberrations, particularly evident before prophase. These compounds are thus radiomimetic in that they are inhibitors of mitosis and mutagenic agents. The main factor determining the sensitivity of a tumour to such drugs is its inherent rate of growth, and in order to obtain the maximum radiomimetic effect with the minimum of toxic complications and damage to the bone marrow it is recommended that fractionated doses should be given rather than a large single dose.

At the Peter MacCallum Clinic, Melbourne, a group of 15 patients with advanced cancer and 4 with malignant lymphoma have been treated with nitromin. The former group included cases of fibrosarcoma (2), malignant melanoma (2), embryoma of the kidney (1), and carcinoma of the colon (3), bronchus (1), cervix uteri (1),

breast (4), and kidney (1). In the cases of fibrosarcoma and malignant melanoma there were skin nodules and lymph-node enlargement. Of the 10 cases of various types of carcinoma, marked regression occurred in 3, but it is noted that in 5 of the remaining cases liver metastases were already present before starting treatment. The patient with an embryonic renal tumour and the 2 with lymphosarcoma showed no response, while there was only partial response in 2 cases of Hodgkin's disease. Two of the patients who responded to nitromin had previously failed to respond to thioTEPA (triethylene thiophosphoramide). "Synkavit" or prednisolone was given concurrently in some resistant cases, in the hope that they would act as sensitizers to the radiomimetic action of nitromin.

I. G. Williams

1226. Therapeutic Trial of *p*-(Di-2-chloroethylamino)-phenylbutyric Acid in Hodgkin's Disease, Chronic Lymphatic Leukaemia and Various Sarcomata of Lymphoid Tissue. (Essai de traitement par l'acide *p*-(di-2-chloro-éthylamino)-phénylbutyrique de la maladie de Hodgkin, de la leucose lymphoïde chronique et de divers sarcomes du tissu lymphoïde)

J. BERNARD, G. MATHÉ, and M. WEIL. *Revue française d'études cliniques et biologiques* [Rev. franç. Ét. clin. biol.] 1, 1121-1132, 4 figs., 13 refs.

The clinical response to the cytotoxic drug *p*-di-(2-chloro-ethylamino)-phenylbutyric acid (chlorambucil) has been studied at the Hôpital Hérold, Paris, in 54 patients with Hodgkin's disease, 28 with chronic lymphatic leukaemia, and 18 with other types of reticulo-endothelial disorder. Chlorambucil was given alone in 69 cases and in combination with cortisone or prednisone in 31. Serious side-effects were infrequent, but leucopenia was common and pancytopenia developed in 3 cases. The dosage was 0.1 to 0.2 mg. per kg. body weight daily by mouth, up to total amounts ranging from 200 to 800 mg. over periods of 10 to 90 days.

In the patients with Hodgkin's disease the pruritus and fever responded well, but the splenomegaly and adenopathy to a lesser degree. In some cases improvement was noted after radio-resistance had developed. Over-all, a definite improvement was observed after about 60% of treatments, one remission lasting as long as 8 months. Among patients with other reticuloses about half responded. In those with chronic lymphatic leukaemia, however, the response was significantly better, improvement resulting after 92.5% of treatments. The combination of chlorambucil and cortisone was considered to be even more effective, and the toxic effects were also fewer. For the treatment of diffuse forms of Hodgkin's disease and of chronic lymphatic leukaemia the authors prefer chlorambucil to radiotherapy. This substance is less toxic than other mustard compounds, such as triethylene melamine. [The duration of follow-up is not stated.]

Kenneth Gurling

1227. Antileukemic Action of Reserpine

A. GOLDIN, R. M. BURTON, S. R. HUMPHREYS, and J. M. VENDITTI. *Science* [Science] 125, 156-157, Jan. 25, 1957. 1 fig., 6 refs.

Infectious Diseases

1228. **The Epidemic Occurrence of a Hitherto Unknown Form of Viral Meningitis and Its Causal Agent.** (Über das epidemische Auftreten einer bisher unbekannten Virus-meningitis und ihrer Erreger)

W. HENNESSEN. *Deutsch medizinische Wochenschrift* [Dtsch. med. Wschr.] **81**, 2088-2090, Dec. 21, 1956.

An epidemic of meningitis due to a hitherto unknown virus occurred in Western Europe between July and October, 1956, affecting mainly children and adults living in inadequate and unhygienic conditions. The course of the infection was benign and short.

At the Düsseldorf Academy of Medicine the author succeeded in isolating a virus from the sputum and faeces of patients and was able to demonstrate neutralizing antibodies to this virus in the patients' serum, the titre showing a considerable increase during the illness. Although the virus was apathogenic for mice, rats, and guinea-pigs, the author himself contracted an infection in the course of experiments with the isolated virus. The incubation period was 5 days and was followed by severe frontal headache, rise of temperature, and the appearance of a small papular erythema of the trunk which was visible for 24 hours. The cerebrospinal fluid was under pressure, and the cells were increased in number and consisted mainly of lymphocytes. The properties of the virus were different from those of the poliomyelitis and Coxsackie viruses, and it is assumed to be of a new type. Antibiotics had no effect upon the virus either *in vitro* or *in vivo*.

Franz Heimann

1229. **The Epidemic of Abacterial Viral Meningitis in the Summer of 1956.** (Über die im Sommer 1956 epidemische aufgetretene abakterielle Virusmeningitis)

H. ODENTHAL and M. WUNDER. *Deutsche medizinische Wochenschrift* [Dtsch. med. Wschr.] **81**, 2090-2093, Dec. 21, 1956. 1 fig., 4 refs.

The authors describe the epidemic occurrence in the summer of 1956 of a form of abacterial meningitis, presumably viral, which resembled the meningitic form of poliomyelitis except that its course was shorter and more benign [see Abstract 1228]. In 26 cases seen at the First Medical Clinic, Düsseldorf Academy of Medicine, the ratio of males to females was 2.5:1.

The onset was not very characteristic, being usually marked by nausea, vomiting, frontal headache, retrobulbar pain, and fatigue with fever. In 15 out of 26 cases the temperature showed a double peak, falling to normal on the 3rd or 4th day and rising again on the 5th, this stage being accompanied by meningitic symptoms which subsided without complications after a few days, the temperature becoming normal in about 10 days. The cerebrospinal fluid (C.S.F.) was clear and colourless, though sometimes a fine "cobweb" coagulum formed on standing similar to that found in tuberculous meningitis. The sugar content of the C.S.F. was normal, but

the protein content showed a moderate increase. There was usually a pleocytosis averaging about 2,000 cells per c.mm., compared with about 500 per c.mm. in poliomyelitis. The complement-fixation test for poliomyelitis was negative. Five patients showed a temporary muscular paralysis which very quickly subsided. No treatment was necessary apart from lumbar puncture for relief of pressure.

Franz Heimann

1230. **Interstitial Pneumonia in Poliomyelitis.** (La pneumonie interstitielle dans la poliomyélite)

G. MARINESCO, N. DRAGANESCU, I. TURCO, I. FRIEDMAN, V. CIUREZO, and P. ROMAN. *Presse médicale* [Presse méd.] **64**, 2207-2210, Dec. 25, 1956. 16 figs., 21 refs.

The authors discuss the clinical and pathological findings in 62 fatal cases of poliomyelitis occurring in Bucharest during the years 1950-5. In 48 cases the patient was less than 7 years, and in 38 less than 3 years old. The predominant clinical type, which occurred in 86.5%, was of the ascending variety.

Examined macroscopically, the lungs showed bronchopneumonic changes in 19 cases, pulmonary congestion in 22, pulmonary haemorrhages in 5, and collapse, massive emphysema, and tuberculosis in one case each. In the 33 cases in which the lungs were examined microscopically the lesions seen could be divided into 3 types: (a) bronchopneumonia (11 cases), (b) interstitial pneumonia (10), and (c) mixed forms (7), while 5 other cases showed simple atelectasis. The bronchopneumonic form differed in no way from other varieties of bronchopneumonia. The interstitial type was characterized by infiltrations of mononuclear cells, including lymphocytes, histiocytes, plasmacytes, and fibroblasts. In 2 cases large macrophages measuring 30 to 50 μ were seen. Patchy atelectatic areas were also noted, the lumen of the bronchi containing mucus infiltrated with lymphocytes. Mixed forms showed features of both the above types. Lesions of the interstitial type occurred in infants under 3 years old in 70% of cases. The maximum incidence of this complication was seen during the first week of illness.

The authors comment that the intensity of the interstitial type of reaction in the lungs paralleled that of the reaction in the nervous system and myocardium. In cases of poliomyelitis of the ascending nervous type vascular changes were most marked, while in the encephalitic type peribronchial infiltration was most intense. They speculate as to the cause of these complications and ascribe them to a viscerotropic form of virus, to the initial viraemia, or to the aspiration of buccopharyngeal secretions in the ascending type.

[The predominance of cases of the ascending type and the absence of conclusive evidence of infection with poliomyelitis virus make the diagnosis of these cases questionable. The specificity of the lung changes is therefore open to doubt.]

I. M. Librach

Tuberculosis

1231. Masked Manifestations of Tuberculosis. (О маскированных проявлениях туберкулеза)

A. I. STRUKOV. *Клиническая Медицина [Klin. Med. Mosk.]* 34, 20-30, No. 12, Dec., 1956. 8 figs., 32 refs.

The recognition of tuberculosis as a general disease is based on (1) the circulation of the infecting organism in the blood stream, and (2) what the author terms "para-specific" reactions as the result of changes in the reactivity of the organism. It is well known that some tissues and organs are specially liable to attack, while others are not; on the other hand, local changes occur in organs not attacked by the specific organism but affected by reactive processes in the body as a whole. These may be of an inflammatory or of a dystrophic character, and occur usually in the mesenchyme. Again, in some forms of tuberculosis well-marked local tuberculous lesions may produce few general symptoms, whereas in other forms the general symptoms overshadow the local lesion. For this reason the tuberculous origin of a general disease may not be recognized.

These "para-specific" manifestations are classified as follows. (1) Neurodystrophic and endocrine, exemplified by disturbances of reflex arcs in which mediastinal nerves are often involved, such as the vagus, or the fibres innervating the capillaries of the bronchial walls. Also the association of thyrotoxicosis with tuberculosis, the former often preceding the clinical appearance of the latter, is an example of a reactive response to a tuberculous invasion. (2) Cardiovascular. Examples of this type of manifestation are thrombo-vasculitis, angioneurosis, escape of plasma, coronary thrombosis, focal and diffuse myocarditis, vascular changes in the renal glomeruli, and nephrosclerosis occurring in the course of acute tuberculosis. (3) Haematopoietic. Reticulo-endothelial proliferation in the bone marrow or liver, leukaemoid reactions (especially in acute haematogenous tuberculosis), haemorrhagic diatheses, sarcoidosis, and even blastomatosis and reticulosarcoma have been observed in the course of acute tuberculosis. (4) Polyserositis. Articular synovitis and obliterative pericarditis are cited as examples of this group.

The author suggests that it may be possible to add further manifestations to this list, to include such conditions as the lieno-hepatic type of tuberculosis, which has as its basis a similar "para-specific" reactive change. The so-called "atypical" forms of tuberculosis are, in the author's view, forms of tuberculosis in which "para-specific" reactions play a large part in masking the local lesion. He concludes that the next most pressing problem is to study the laws which govern these reactions, so that the pathology of tuberculosis in all its forms can be fully understood.

[Erythema nodosum, which may be regarded as being a similar manifestation, is not referred to.]

L. Firman-Edwards

RESPIRATORY TUBERCULOSIS

1232. The Effects of Corticotropin (ACTH) and Cortisone in Fifteen Cases of Pulmonary Tuberculosis

E. J. DES AUTELS, J. R. ZVETINA, G. S. BERG, J. FERSHING, and S. FREEMAN. *Diseases of the Chest [Dis. Chest]* 30, 486-498, Nov., 1956. 4 figs.

At the Veterans Administration Hospital, Hines, Illinois, 15 cases of advanced tuberculosis were treated with ACTH (corticotrophin) or cortisone in various dosages for 4 to 33 weeks. Whereas all but 5 of the patients had had chemotherapy for one to 10 months previously, none had adequate chemotherapy during the period of hormone therapy. In most cases there was dramatic clinical improvement which, however, contrasted sharply with the radiological deterioration observed in many. There were 3 deaths during hormone treatment and 4 further patients died within 4 months of the period of treatment, 10 of the 15 having died by the time of the report. The authors conclude that "cortisone was usually harmful and never beneficial; whereas ACTH may have been beneficial in an occasional case, of equivocal effect in some, and probably harmful in the majority".

[There is no discussion of the ethical aspects of this astonishing experiment.]

C. M. Fletcher

1233. Isoniazid Alone in the Treatment of Pulmonary Tuberculosis.

F. V. JIMENEZ. *American Review of Tuberculosis and Pulmonary Diseases [Amer. Rev. Tuberc.]* 74, 903-916, Dec., 1956. 4 figs., 32 refs.

The work here reported was carried out at the Hospital Dos de Mayo, Lima, Peru, where the author observed the results of the long-term treatment with isoniazid alone of some 40 patients with pulmonary tuberculosis. From all these patients tubercle bacilli were isolated; none had received chemotherapy previously or were given collapse treatment once isoniazid therapy, which was continued for at least 9 months, had been started. The patients were rested either at home or in hospital and the radiological progress of the disease was checked every 3 months. The sputum was held to have become negative when 3 cultures taken at intervals of one month were negative and no tubercle bacilli were seen in smears. A cavity was considered to have closed when it could no longer be seen on tomography. Bacterial sensitivity to isoniazid could be determined in only a few cases, and the results are not reported. The drug was given by mouth 3 times a day, the total daily dosage being based on 5 or 10 mg. per kg. body weight.

Of the 55 patients accepted for the investigation, 12 were eventually discarded because of change in treatment or failure to attend for examination. This left

43 patients who received isoniazid for at least 9 months, though in fact 36 received it for 12 months and 29 for 15 to 21 months; 34 patients have been followed up for 2 years. In 22 cases the patient started with a daily dose of 10 mg. per kg. and 21 with 5 mg. per kg.; 40 were male and 3 female; 34 were less than 30 years old and 9 were older; the disease was advanced in 26 cases, with multiple cavities in 16 and at least one lobe being destroyed in 8; non-pulmonary complications were present in 14.

The results of treatment (no distinction being made between doses of 5 and 10 mg. per kg.) were as follows. Radiological improvement was found at 6 months in 26 of 43 patients (60%) and at 2 years in 32 of 34 patients (95%). Radiological deterioration had occurred in 3 cases (7%) at 6 months and in 3 (9%) at 2 years. Cavities were closed in 8 cases (21%) at 6 months and in 22 (71%) at 2 years. The sputum had become negative in 27 cases (63%) at 6 months and in 28 (83%) at 2 years; the sputum had become positive again in 2 cases (6%) at 2 years. In only one case did relapse occur when the patient was taking isoniazid; in the other instances the relapse occurred after the patient stopped treatment. The non-pulmonary tuberculous lesions all healed during treatment. The only instance of isoniazid toxicity, peripheral neuritis, appeared during the ninth month of treatment.

The author suggests that these results are comparable with those obtained with combined chemotherapy and that the use of isoniazid alone, particularly in the higher dosage, should be studied further. *Arthur Willcox*

1234. Serum Isoniazid Levels and Catalase Activities of Tubercle Bacilli from Isoniazid-treated Patients

W. MANDEL, M. L. COHN, W. F. RUSSELL, and G. MIDDLEBROOK. *American Journal of the Medical Sciences [Amer. J. med. Sci.]* 233, 66-68, Jan., 1957. 11 refs.

1235. Pulmonary Tuberculosis in North Glasgow. An Epidemiological Study

W. F. TYRRELL and J. SMITH. *British Medical Journal [Brit. med. J.]* 2, 1451-1455, Dec. 22, 1956. 10 refs.

The authors report the results of a personal investigation into the socio-economic status of 125 patients over 14 years of age with active adult-type pulmonary tuberculosis discovered during a recent 12-month period in the northern area of Glasgow, an area which contains about 250,000 people, mostly of the working class. Practically all the cases were sputum-positive. Distribution of the cases according to age, sex, and race revealed nothing of special significance (only 4 patients came from Ireland and 4 from the Scottish Highlands). Most of the patients were of the artisan class, but 16 of them were employed in the preparation or distribution of foodstuffs. In approximately three-quarters of both the male and female cases there was a history of contact with other tuberculous patients. Overcrowding was observed in 18% of the households concerned, but neither this nor the type of dwelling appeared to have any material bearing on the incidence of the disease; nor was poverty a serious factor, for the great majority of

patients belonged to homes with a total family income of between £10 and £20 a week.

Out of 412 household contacts examined (94.6% by Mantoux testing and 99.5% by radiography), 21 were found to have active pulmonary tuberculosis and a further 31 to have suspected or quiescent disease. These figures, when compared with the incidence disclosed by mass radiography (usually some 5 per 1,000) add to the existing evidence for the importance of examination of contacts in all cases of pulmonary tuberculosis.

[This survey provides interesting information on the decreasing importance of socio-economic factors previously regarded as vital in the epidemiology of tuberculosis, particularly housing conditions and poverty. But the danger of personal contact with active cases is all the more evident.] *R. J. Matthews*

1236. Ototoxicity from Intermittent Streptoduocin Therapy of Pulmonary Tuberculosis. A Study of One Hundred Five Patients Treated Eight to Ten Months

J. A. WIER, P. B. STOREY, F. J. CURRY, and J. M. SCHLESS. *Diseases of the Chest [Dis. Chest]* 30, 628-632, Dec., 1956. 2 refs.

Mixtures of equal parts of streptomycin and dihydrostreptomycin are now available for the treatment of pulmonary tuberculosis, and the authors have evaluated the toxic effects of the use of such a mixture ("streptoduocin") on the auditory and vestibular function of 105 young adult males under treatment at the Fitzsimons Army Hospital, Denver, Colorado. Streptoduocin was given intramuscularly in a dosage of 2 g. every third day for the first 6 months and then 1 g. every third day for a further 2 to 4 months, isoniazid and/or PAS being given orally simultaneously. The results were compared with those in an earlier series of patients from the same hospital who were treated with streptomycin only, as previously described (Cline *et al.*, *A.M.A. Arch. Otolaryng.*, 1954, 59, 100).

The incidence of vestibular damage alone, which in the 1954 series was appreciable (12%) but compensated for, was in the present series reduced to about one-quarter (2.8%), but there were 4 cases of clinical deafness, and audiometry indicated that 37% of the patients had some loss, particularly in the higher frequencies, compared with only 12% in the earlier series.

The authors conclude that the increase in damage to the auditory nerve which is associated with the use of dihydrostreptomycin is sufficient to outweigh the theoretical advantages of its use in a mixture with streptomycin. *J. Robertson Sinton*

1237. Pulmonary and Circulatory Function of the Re-expanded Pneumothorax Lung

J. RAKOWER, O. J. BALCHUM, and S. H. DRESSLER. *Diseases of the Chest [Dis. Chest]* 30, 649-658, Dec., 1956. 19 refs.

The problem of the extent to which lungs collapsed by the induction of pneumothorax recover their function now affects a steadily diminishing number of patients because of the current trend away from this form of treatment. But this report from the National Jewish

Hospital, Denver, Colorado, amplifies information available from earlier studies and reports the results of the investigation of pulmonary function in 47 cases examined several years after the abandonment of the pneumothorax. It confirms that some loss of function occurs in respect of vital capacity, maximum breathing capacity, and oxygen uptake, and that although the loss is unpredictable with any certainty, it is more likely to be severe in cases in which empyema and fibrothorax had occurred than in uncomplicated cases. That in patients with severe contralateral disease the re-expanded lung, in spite of diminished vital capacity and maximum breathing capacity, may show unexpected ability to increase oxygen uptake by increasing the pulmonary arterial pressure is suggested by the findings in 6 cases in which cardiac catheterization was carried out.

J. Robertson Sinton

1238. U.S. Veterans Administration-Armed Forces Cooperative Studies of Tuberculosis. V—Antimicrobial Therapy in the Treatment of Primary Tuberculous Pleurisy with Effusion: Its Effect upon the Incidence of Subsequent Tuberculous Relapse

A. FALK and W. W. STEAD. *American Review of Tuberculosis and Pulmonary Diseases* [Amer. Rev. Tuberc.] 74, 897-902, Dec., 1956. 2 figs., 2 refs.

A study of antimicrobial therapy in primary tuberculous pleurisy with effusion was carried out at the Veterans Administration Hospital, Minneapolis. The criteria for diagnosis were: (1) a recent effusion, preferably present less than 60 days; (2) tuberculin skin reaction positive before or during treatment; (3) "tubercle bacilli should, when possible, be demonstrated in the aspirated fluid by culture or guinea-pig inoculation" [but since failure to do so was apparently not regarded as a reason for exclusion, this should surely not be counted among the diagnostic "criteria".—EDITOR]. Patients with a parenchymal lung lesion were excluded. Altogether, 382 patients received chemotherapy of some kind, 12 receiving streptomycin alone, 250 streptomycin and PAS, and 120 isoniazid and streptomycin or isoniazid and PAS. The duration of chemotherapy ranged from less than 4 to more than 6 months. A control series of 209 patients who had no chemotherapy was also studied, the constitution of the two groups being very similar in that in each approximately 95% were males, half were under 30 years of age, and two-thirds were white.

Both groups were followed up for 4 years. Recurrent pleural effusion occurred in 1% of the treated group and in 5% of the untreated group (this difference not being statistically significant), while other tuberculous complications occurred in 4% of the treated group and in 19% of the untreated group. Pulmonary tuberculosis was the commonest complication, with skeletal tuberculosis next in order, but very much less frequent.

Other impressions gained, but not proven statistically, were that extrapulmonary complications were less common in the untreated group, and that among the patients given chemotherapy fewer complications occurred in those who received a combination of drugs which included isoniazid. It is noted that no tubercle bacilli

had been found in the pleural fluid of most of the patients, in both groups, who later developed recurrent effusions or other complications.

Arthur Willcox

1239. An Association between Smoking and Respiratory Tuberculosis

C. R. LOWE. *British Medical Journal* [Brit. med. J.] 2, 1081-1086, Nov. 10, 1956. 4 figs., 9 refs.

In England and Wales it is notable that the decline in mortality from respiratory tuberculosis has affected males in older age groups less than females or young males, so that the age-mortality curves now show a marked sex differential, with peaks at 15 to 24 years in females and 55 to 64 years in males. The distribution of notification rates by age for males has become bimodal, with peaks at 20 to 24 and 50 to 54 years, while for females there is a steady decline after 24 years. Attempts to explain this sex difference, with an excess of notified or fatal disease in elderly males, as a cohort effect or as due to the proportion of males in industry, are unsatisfactory. It is becoming accepted (see Springett, *Lancet*, 1952, 1, 521 and 575; *Abstracts of World Medicine*, 1952, 12, 182) that a large part of the tuberculosis occurring in males in later life is due to breakdown of foci of disease acquired earlier.

During 1955 the author investigated the smoking habits at the time of notification of patients in the three principal sanatoria in Birmingham and of patients attending the Birmingham Chest Clinic for respiratory tuberculosis, a total of 1,200 patients (males 763, females 437). A control series of 979 consisted of patients attending hospital with minor injuries and of patients occupying beds in a general hospital for causes other than lung cancer and respiratory tuberculosis (males 564, females 415). There was an excess of moderate and heavy smokers among patients of both sexes aged over 30 with respiratory tuberculosis as compared with the controls—11.7% of tuberculous males smoked fewer than 10, and 50.1% 20 or more cigarettes daily, compared with 21% and 43.4% respectively for the controls. There was little difference in smoking habits between the sanatorium and chest-clinic patients or between the two control groups. Similar results were obtained for each 10-year age group, but in the age group 20 to 24 years there was no appreciable difference between the smoking habits of patients and controls.

The author advances the hypothesis that the sex difference in the age-incidence and age-mortality curves of respiratory tuberculosis, being due to a re-activation of old infection in elderly males, has a marked association with smoking habits. In further support of this, the ratio of male to female deaths from respiratory tuberculosis in England and Wales in the age group 45 years and over is shown to have climbed steeply since the decade 1911-20, at which time consumption of tobacco also began to increase rapidly.

R. H. Cawley

1240. Pulmonary Resection for Tuberculosis. A Five-to Ten-year Follow-up Study

J. D. MURPHY and J. M. DAVIS. *Journal of Thoracic Surgery* [J. thorac. Surg.] 32, 772-775, Dec., 1956.

Venereal Diseases

1241. Oral Phenoxymethyl Penicillin in Acute Male Gonorrhoea

L. P. SHEIL. *British Journal of Venereal Diseases* [Brit. J. vener. Dis.] 32, 251-252, Dec., 1956. 2 refs.

At St. Thomas's Hospital, London, 28 male patients with acute gonorrhoea were treated with phenoxymethyl penicillin (penicillin V) by mouth in doses of 1.2 mega unit each day for 3 days combined with daily urethral irrigation with potassium permanganate solution (1 in 8,000) for 14 days. One patient had loose bowel motions, but otherwise there were no toxic effects. Two patients defaulted, one after receiving only one dose and the other after only two.

The diagnosis was made on examination of a stained smear in every case; the gonococcal complement-fixation reaction before treatment was negative in 23 cases, doubtfully positive in 2, and strongly positive in 3. Urethral smears were free from gonococci on the second day in all 27 cases examined and remained so, except in one case of re-infection, for follow-up periods which ranged up to 115 days. In 20 cases prostatic beads were examined from 21 to 91 days after treatment; of these 17 were normal, 2 contained pus, and gonococci were present in one. The author claims that these results appear to be as good as those obtained concurrently in 102 cases of gonorrhoea treated with intramuscular injections of 500,000 units of procaine penicillin.

[Oral treatment of gonorrhoea with penicillin is certainly effective, but this report illustrates the risk of insufficient dosage through failure to take the full course of the drug, and the necessity for efficient tests.]

Robert Lees

1242. Intradermal Tests in the Diagnosis of Lymphogranuloma Venereum

A. J. KING, C. F. BARWELL, and R. D. CATTERALL. *British Journal of Venereal Diseases* [Brit. J. vener. Dis.] 32, 209-216, Dec., 1956. Bibliography.

The incidence of positive reactions to intradermal tests for lymphogranuloma venereum among 1,317 patients attending the Whitechapel Clinic of the London Hospital between November, 1954, and December, 1955, was first determined, and then those patients giving a positive reaction were studied with a view to establishing or excluding a diagnosis of lymphogranuloma venereum. Antigen prepared from yolk-sac culture of the J.H. strain of lymphogranuloma venereum virus was used, the virus being inactivated by heat instead of by phenol or urea; this is a group antigen giving a positive reaction not only in cases of lymphogranuloma, but also in cases of infection with the psittacosis group of viruses. In every case a control antigen prepared from uninfected yolk sac was employed. An inflammatory papule at least 6 mm. in diameter after 48 hours, with absence of response to control antigen, was regarded as a positive result.

Assessment was possible in 1,119 cases, and in 206 (18.4%) of these there was a positive reaction to the intradermal test. In addition a strongly positive reaction to the complement-fixation test was obtained in 23 cases (2% of total), confirming a diagnosis of lymphogranuloma venereum, although only 10 had clinical signs of the disease. A further 157 positive reactors to the intradermal test had complement-fixing antibodies in the blood, but not in sufficient quantity to justify a firm diagnosis of active infection. Compared with the white patients the relatively small number of negroes in this series showed proportionately a higher incidence both of doubtful and proved infections. In 63 patients tests were carried out with a commercial antigen ("lygranum") and London Hospital antigen simultaneously; no marked discrepancy between the results was observed.

The authors conclude that there is an appreciable incidence of lymphogranuloma venereum remaining undiagnosed among the population of the East End of London.

A. J. Gill

SYPHILIS

1243. The Serological Differentiation between Congenital Syphilis and Placental Transmission of Maternal Reagins. (Zur serologischen Differentialdiagnose zwischen Lues connata und diaplazentar übertragenen mütterlichen Reaginen)

F. MÜLLER. *Archiv für Kinderheilkunde* [Arch. Kinderheilk.] 154, 153-162, 1956. 18 refs.

The interpretation of the results of serological tests on the clinically healthy child of a syphilitic mother raises serious therapeutic and prophylactic problems. The author states that when the Wassermann reaction (W.R.) is positive in both mother and child, the Meinicke reaction (M.K.R. II) will be negative in the non-infected child, even though it is positive in the mother, since the reagin concerned is not transmitted transplacentally. On the other hand the M.K.R. II is the first reaction to become positive in adult infection, and, assuming that the evolution of intra-uterine infection parallels that of the adult, a positive M.K.R. II in the newborn infant, even with a negative W.R., would indicate congenital syphilis.

The serological findings in a series of 202 cases of maternal syphilis are here reported from the Paediatric Clinic of the University of Hamburg, the results being presented in the form of tables. The M.K.R. II was positive in 52 (84%) of the 62 newborn children with signs of congenital syphilis and in 12 (8%) of the 140 children who had no clinical signs of the disease, and it is assumed that these 64 infants had congenital syphilis. Proof is impossible to furnish, however, because all the children were given at least one course of prophylactic

treatment, though some collateral evidence is provided by the fact that on treatment the W.R. titres fell rapidly in the M.K.R. II-negative children and very much more slowly in those with a positive M.K.R. II. The importance of maternal treatment during pregnancy is evidenced by the fact that all but one of the children with positive clinical signs or serological reactions or both were born of untreated or insufficiently treated mothers. It is emphasized that a negative M.K.R. II in the child of an untreated syphilitic mother should not be held to exclude congenital syphilis.

Since the W.R. with cardiolipin antigen is not a satisfactory means of distinguishing passively transmitted reagins from those due to active infection of the child, while the transplacental transmission of treponemal immobilizing antibody has also been demonstrated, it is therefore suggested that the M.K.R. II should invariably be carried out in the investigation of congenital syphilis.

F. Hillman

1244. Report of Syphilis Follow-up Program among Veterans after World War II

S. R. TAGGART, S. B. RUSSELL, and E. V. PRICE. *Journal of Chronic Diseases* [J. chron. Dis.] 4, 579-588, Dec., 1956. 3 figs.

Between 1940 and 1946 approximately 500,000 members of the U.S. Armed Forces had acquired or had been treated for syphilis. The authors, on behalf of the Veterans Administration, undertook a study of the current status of a proportion of these cases. The actual investigations were conducted by State and local health departments in cooperation with the U.S. Public Health Service; as it was impossible to investigate all the 500,000 cases only the following patients were included: (1) those whose cerebrospinal fluid (C.S.F.) had not been examined; (2) those with previously recorded positive or doubtful findings in the C.S.F.; and (3) those who had received "inadequate" treatment; as a result of this selection the number of patients was reduced to some 122,000.

The follow-up programme was carried out for a period of approximately 3 years from 1950, a total of 122,461 questionnaires being sent to State health departments, of which 90,293 (73.7%) were returned; from these 81,715 patients were selected for further investigation. Of this number, however, 45% could not be traced, 12% were unwilling to submit themselves to examination, 3% were still in military service, 0.7% were dead, and 5% were not investigated for various other reasons.

Of the remaining 34% (27,786 subjects) who were located, all underwent blood tests and almost half examination of the C.S.F. In 18.8% a serological test for syphilis (S.T.S.) gave a positive result and in 2.7% a doubtful result. The C.S.F. reaction was positive or doubtful in 4.2% of those examined. The sample selected for final analysis consisted of those "who had not had a lumbar puncture in the Services", and who had been diagnosed as having primary or secondary syphilis; with all these limitations the final group numbered 8,317. Of the 140 with a positive C.S.F.

reaction, 49 (39%) had a negative S.T.S. reaction. In general the longer the period between initial treatment and follow-up, the higher the percentage of those with a positive C.S.F. reaction. Patients with more recent infections had been treated with penicillin, those with the earliest had received arsenoxide and bismuth, while the two methods of treatment had overlapped in those examined 6 to 8 years after treatment. Of those treated with penicillin, 2.88% had a positive C.S.F. reaction, compared with 2.07% of those treated with arsenoxide and bismuth, suggesting that penicillin was no more effective in preventing neurological involvement than the older treatment. Differences in the types of penicillin used at varying periods are discussed. Among patients treated with penicillin K the rate of neurological involvement was 3%, as against 0.4% among those treated with benzylpenicillin.

On the basis of these findings it is estimated that a minimum of 15,000 U.S. veterans of World War II would show evidence in the C.S.F. of neurosyphilis at the present time.

Douglas J. Campbell

1245. Late Hepatic Syphilis

I. A. KELLOCK and S. M. LAIRD. *British Journal of Venereal Diseases* [Brit. J. vener. Dis.] 32, 236-241, Dec., 1956. 1 fig., 17 refs.

Evidence in the recent literature indicates that the incidence of late syphilitic disease of the liver is low. Estimates on clinical grounds are not very reliable, but necropsy studies of unselected series give an incidence varying between 0.36% (of 53,028 cases) and 1.5% (of 3,300 cases), while among adult syphilitics an incidence of 4.9% (of 1,165 cases) has been reported. The clinical diagnosis of this condition is never easy, but with the advent of penicillin the therapeutic test, which has long been recognized as a useful aid to diagnosis, has become safer and more decisive.

The present authors report 7 cases of late hepatic syphilis from Manchester Royal Infirmary, in one of which the lesion was probably a solitary gumma, while the remainder were examples of diffuse liver disease. They point out that some difficulty in diagnosis may arise from the fact that the standard serological tests for syphilis may be upset by disturbance of the blood proteins in non-syphilitic disease of the liver. But a negative treponemal immobilization reaction and a lack of clinical evidence of syphilis should eliminate a false positive diagnosis of syphilis in such cases. They emphasize that the therapeutic test is probably the most valuable single diagnostic procedure, as liver function tests and needle biopsy may not give helpful or conclusive results. But they state that for the diagnosis to be certain the initial improvement must be maintained during an observation period of many months or preferably several years. Penicillin therapy is advised as the best method of treatment, though even with this drug satisfactory results will depend on treatment being started before the disease is too far advanced. Syphilis may be too readily overlooked in the differential diagnosis of liver disease, and should be suspected in all cases of hepatic and splenic enlargement.

Robert Lees

Tropical Medicine

1246. **Kwashiorkor in Sicily.** (Il kwashiorkor in Sicilia)

M. GERBASI. *Pediatrics* [*Pediatrics (Napoli)*] **64**, 941-1004, Nov.-Dec., 1956. 34 figs., bibliography.

In this paper from the Paediatric Clinic of the University of Palermo 20 cases of kwashiorkor occurring in white children are considered in detail and the findings analysed. The ages of the children ranged from 4 months to 5 years, most being between 6 and 24 months old. The majority of cases came from the families of labourers. The incidence was mainly from July to November. Definite deficiency of animal protein was present in 7 cases only, and 5 were on a milk diet. The importance of infectious diarrhoea in precipitating the condition is stressed, such diarrhoea being apparently a cause and not the result of kwashiorkor in Sicily.

Apathy, skin lesions (especially on the perineum or resembling those of pellagra), straight, dry hair, and oedema are considered typical clinical features. The treatment in these cases included a moderately high-protein diet, blood transfusions when necessary, and the administration of liver extract, vitamins, and antibiotics, aureomycin being of special benefit. The response was good.

[The original article should be consulted by workers in this field, being too long to abstract. Some of the data given—for example, comparisons of height and weight with those of normal children—are not easily available for many parts of the world. An account of haematological and biochemical studies is included, together with a good review of the literature.]

W. H. Horner Andrews

1247. **Oral Absorption Tolerance Tests in Tropical Sprue**
F. H. GARDNER and E. P. SANTIAGO. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **98**, 467-474, Oct., 1956. 4 figs., 21 refs.

From the Tropical Research Medical Laboratory, U.S. Army, San Juan, Puerto Rico, the authors report the results of a study of the rate of absorption of sugars and fats in 55 patients (aged between 13 and 78 years) with tropical sprue. The tests were made before and after treatment with folic acid (usually 5 mg. daily) supplemented in some cases with iron therapy. Four older patients with achlorhydria received weekly intramuscular injections of 30 µg. of cyanocobalamin instead of the folic acid. For the sugar absorption test the authors gave 25 g. of D-xylose in 500 ml. of water by mouth and estimated the amount of this pentose excreted hourly in the urine for 5 hours. To evaluate fat absorption two methods were used: (1) vitamin-A tolerance by giving 300,000 i.u. of the vitamin orally to a fasting patient and determining the serum levels before, and 5 and 7 hours after, administration; and (2) butter-fat absorption by giving 30 g. of butter with breakfast and

estimating the serum turbidity in 5-hourly samples of blood.

The results of the absorption tests are presented graphically. There was a generalized marked depression in absorption of the test substances before treatment, and, although a good haematological and clinical response to treatment was apparent, there was only minimal improvement in the absorption rate. The authors conclude that "such studies would indicate that tropical sprue as observed in Puerto Rico is not a reversible nutritional deficiency". C. L. Pasricha

1248. **Chagas' Disease. A Clinical, Epidemiologic, and Pathologic Study**

F. S. LARANJA, E. DIAS, G. NOBREGA, and A. MIRANDA. *Circulation* [*Circulation (N.Y.)*] **14**, 1035-1060, Dec., 1956. 16 figs., 29 refs.

This study of Chagas's disease from the Instituto Oswaldo Cruz, Rio de Janeiro, is based on evidence from 180 acute cases (21 deaths, 11 necropsies), 657 asymptomatic chronic infections, and 683 cases of chronic Chagas's heart disease (21 in which *Trypanosoma cruzi* was found in the myocardium post mortem).

Cases of acute infection are more frequent in the summer months and may occur at any age, but usually in the first years of life. Over 60% of the cases studied occurred between 1 and 5 years. The clinical picture is readily recognized in endemic areas, with general malaise, fever, abundant sweating, muscular pains, irritation, anorexia, and sometimes vomiting and diarrhoea; local signs of the portal of entry of the parasite, lymph-node enlargement, generalized oedema, and in some cases anasarca; hepatomegaly and moderate splenomegaly; and occasionally cutaneous eruptions. Symptoms and signs of heart involvement, and in some cases (usually fatal) symptoms of involvement of the central nervous system (acute meningoencephalitis) occur during the acute phase. Cardiac involvement probably occurs in almost every acute case, but is frequently not recognized. Serial x-ray examinations of the chest and electrocardiography are the most accurate methods for the detection of this complication.

The authors state that diagnosis is based on the demonstration of the parasite by microscopical examination of the blood (though after 6 to 10 weeks trypanosomes are difficult to find), by xenodiagnosis, by animal inoculation of blood, or by blood culture. The complement-fixation test may yield negative results in the early stages of acute infection, but is a valuable procedure for the diagnosis of chronic Chagas's disease. The acute infection is most severe in early infancy, and in adolescents and adults is rarely fatal. Mortality is about 10%. In treatment a 4-aminoquinoline derivative, "Bayer 7602 (Ac)", and a sulphurated arsenobenzol, "Bayer 9736 (As)", are claimed to possess trypanocidal effects

on the circulating forms, but not on the intracellular forms.

Following the acute stage of the infection there is an asymptomatic period, usually lasting from 10 to 20 years, before the establishment of the late heart disease of chronic infection. In diagnosing chronic Chagas's disease the clinical history is of the utmost importance and detailed information should be obtained on epidemiologic factors operating in the area where the patient was born or has lived. A history of heart disease in other members of the same family or in other young individuals from the same region is commonly elicited. Approximately 55% of fatal cases are in the age group 21 to 40 years, mortality below 20 years of age being low. Prognosis is difficult; sudden and unexpected death is very common in this cardiopathy.

[This paper contains a great deal of clinical and pathological description which cannot be dealt with adequately in an abstract.]

I. M. Rollo

1249. Diphtharsone in the Treatment of Acute Amoebic Dysentery

A. J. WILMOT, S. P. POWELL, and R. ELSDON-DEW. *Journal of Tropical Medicine and Hygiene* [J. trop. Med. Hyg.] 60, 16-18, Jan., 1957. 12 refs.

Diphtharsone (*bis*-(*p*-arsonophenylamino)-1:2-ethane; "bemarsal") has been the subject of a number of clinical trials in intestinal amoebiasis by French workers. In the present study, reported from the University of Natal, 44 African patients suffering from acute amoebic dysentery were treated with 2.5 g. of diphtharsone daily for 10 days.

The immediate results compared favourably with those obtained with other direct amoebicides, 32 (73%) of the patients being considered cured on examination after 27 days. However, at follow-up one month later, 7 out of 25 (28%) of the successfully treated patients showed a recurrence of parasites. No toxic symptoms were encountered. It is concluded that diphtharsone is a useful drug in acute amoebic dysentery, but that it seems likely that it should be used with other anti-amoebic agents, particularly the wide-spectrum antibiotics, if satisfactory immediate results and permanent cure are to be obtained.

R. R. Willcox

1250. Observations on the Value of the Complement Fixation Test in the Diagnosis and Management of Amoebiasis

B. HALL and H. L. CARRUTHERS. *Medical Journal of Australia* [Med. J. Aust.] 1, 32-36, Jan. 12, 1957.

In an investigation of the value of the complement-fixation test in the diagnosis of amoebiasis at the Repatriation General Hospital, Concord, Sydney, the authors used a commercially-prepared antigen and selected 103 cases in which there was active infection, or a history of amoebiasis with continuing clinical evidence of the disease, or infection was suspected. A group of 73 cases in which there was little likelihood of amoebiasis being present served for control purposes.

In 68 of the 103 cases the results of the complement-fixation test were positive or there was evidence of

infection on sigmoidoscopic examination. However, positive and negative results of both the serological test and sigmoidoscopic examination were noted in all groups, and there was no absolute correlation with the presence or absence of parasites in the stools. The complement-fixation test gave a positive result in 5 of the 73 control cases; subsequently 4 patients in this group were found to be harbouring the causative organism. Of 60 patients receiving treatment for amoebiasis, the result of the complement-fixation test changed from positive to negative in 47 and from negative to positive in one; of the remaining 12, in 4 it remained positive and in 8 negative.

The precautions observed during the investigation and the technique for serological testing are described in detail. The authors conclude that the complement-fixation test is "reasonably specific" but that a positive result should be supported by other diagnostic evidence.

[From the authors' findings it would be more accurate to conclude that the only reliable diagnostic test for amoebiasis is microscopical demonstration of *Entamoeba histolytica* in the faeces.]

R. A. Neal

1251. Clinical Studies in the Use of Cortisone and Corticotropin in the Reactive Episodes of Leprosy

J. S. SHUTTLEWORTH. *International Journal of Leprosy* [Int. J. Leprosy] 24, 129-137, April-June, 1956 [received Jan., 1957]. 18 refs.

The author describes his experience at the U.S. National Leprosarium, Carville, Louisiana, with cortisone and corticotrophin (ACTH) in the treatment of reactive episodes in leprosy.

The erythema-nodosum type of reaction occurs in 63% of lepromatous cases and has been more common since the introduction of sulphone treatment. Many drugs have been advocated for this condition, but up to the present the most successful has been stilbophen (fouadin). The most striking histological change in these lesions is endothelial proliferation in the subcutaneous vessels and marked oedema in the corium, suggesting the possibility of an allergic reaction.

Details of 10 cases treated with cortisone in the reactive stage are presented. The dosage of cortisone varied from 25 to 400 mg. daily. In one case in which shock-like symptoms developed after administration of cortisone, ACTH (corticotrophin) was given with benefit. The immediate results were good and in some cases spectacular, but the long-term results were poor. Among the immediate good results the relief of pain in cases complicated by neuritis was most impressive. Hormone therapy had no apparent aggravating effect on the leprosy. In some reactive cases it was possible to continue or resume sulphone therapy after a short course of cortisone. If the untoward features of hormone therapy, such as electrolyte and water retention, as well as withdrawal symptoms are kept in mind the author considers that it has a place in the treatment of leprotic reaction. He considers that such therapy is best given in short courses and is of particular value in cases of neural reaction.

William Hughes

Allergy

1252. **Tree Pollen in Great Britain.** [In English]
H. A. HYDE. *Acta allergologica* [*Acta allerg.* (Kbh.)]
10, 224-245, 1956. 7 figs., 11 refs.

The main findings of a survey begun in 1942 and still continuing, of the incidence of various tree pollens in Britain, with special reference to allergy, are reported. At 9 different stations pollen was trapped throughout one or more seasons, the gravity slide method being used. The findings show that the tree pollen catch is much influenced by the type of vegetation immediately around the station. At Cardiff, where counts have been made for many years, the quantitative incidence of most kinds of tree pollen varies from year to year. This may account for the fact that for the most part tree pollens are not strong sensitizers. A bumper crop may be followed by a very small crop. The actual dates when the tree pollens are abundant in the air vary widely from year to year. Some trees, such as ash, produce a short compact pollen cloud, while others, such as hazel, have a diffuse, long-lasting, but not intense, pollen season. Details are given of tree and shrub pollens caught from the air in Britain which are known or presumed to be antigenic.

[Tree-pollen desensitization should not be undertaken until the considerable amount of information in this article has been mastered.]
A. W. Frankland

1253. **Sputumdiagnosis in Asthma Bronchiale with Special Reference to the Occurrence of a Complicating Bronchial Infection.** [In English]
S. BERGMAN and H. COLDAHL. *Acta allergologica* [*Acta allerg.* (Kbh.)] 10, 63-72, 1956. 3 figs., 7 refs.

In cases of bronchial asthma a sputum regarded as purulent on macroscopical examination may give no indication whether bronchial infection is present or not. When sputum is cultured, however, difficulties arise from contamination by bacteria from the throat and mouth. To eliminate these, Mulder (*Acta med. scand.*, 1938, 94, 98) suggested washing the sputum before culture. May (*Lancet*, 1952, 2, 1206; *Abstracts of World Medicine*, 1953, 14, 49) using a random sampling method, found *Haemophilus influenzae* and pneumococci to be the most important pathogens in chronic bronchitis. The present authors, at St. Görans Hospital, Stockholm, in an attempt to decide the best method of sputum examination, have compared the bacteriological findings by different techniques in the sputum of asthmatic patients. In 5 cases the sputum was examined (1) by ordinary culture methods; (2) by Mulder's method after being washed three times; and (3) after sterile bronchoscopic suction. In a further 31 cases comparison was confined to Methods 1 and 2. With each of the three methods the bacteriological findings varied; details are shown in tables. Brief reports are also given of 3 cases in which indications for treatment were derived

from examination of the sputum by Mulder's method. The authors conclude that washing the sputum enables the truest picture to be obtained of the types of organisms responsible for infective episodes in asthma, especially when there is a raised erythrocyte sedimentation rate. According to them *H. influenzae* is the most important of these organisms.
A. W. Frankland

1254. **A Contribution to the Problem of Autosensitization in Bronchial Asthma.** [In English]
G. BERGQUIST. *Acta allergologica* [*Acta allerg.* (Kbh.)]
10, 187-193, 1956. 6 refs.

Preliminary experiments *in vitro* suggested that the mucous membranes of the nasopharynx could be changed as a result of the growth of *Staphylococcus aureus* and acquire allergenic properties, the nasal mucous membrane being more susceptible than that of the throat. Bacterial samples were taken from the nose of asthmatic patients whose symptoms began with a coryza. When *Staph. aureus* predominated in the flora this organism was grown on a special culture medium made from bouillon and 10% nasal mucous membrane. The patients were subjected to an intracutaneous skin test with a dilution of 1 in 1,000 of the vaccine, and a control test was carried out on healthy non-allergic subjects. Positive skin reactions—that is, an area of oedema twice the size of the control weal produced with saline—were obtained in 28 out of 64 patients tested. In 16 cases there was a positive reaction to an extract of the mucous membrane agar before bacterial cultivation.
A. W. Frankland

1255. **Molar Sodium Lactate in Acute Epinephrine-fast Asthmatic Patients**
J. S. BLUMENTHAL, E. B. BROWN, and G. S. CAMPBELL. *Annals of Allergy* [*Ann. Allergy*] 14, 506-510, Nov.-Dec., 1956. 11 refs.

In studies carried out at the University of Minnesota, Minneapolis, on 2 volunteer asthmatic subjects adrenaline was infused intravenously during a state of alkalosis produced by hyperventilation and then during acidosis produced by breathing 10% carbon dioxide. During alkalosis 12.5 and 15 μ g. of adrenaline respectively caused an increase of the pulse rate from 55 to 114 per minute in one subject and from 114 to 156 per minute in the other, whereas during acidosis doses of 25 and 15 μ g. of adrenaline increased the pulse rate only from 114 to 128 and from 90 to 96 per minute respectively. Because of the much greater effect of adrenaline during alkalosis the authors then gave 120 to 150 ml. of molar sodium lactate intravenously to 22 adrenaline-tolerant or adrenaline-fast asthmatic patients, without any other medication. The results were uniformly good.

The authors suggest that tolerance to adrenaline is the result, at least in great part, of either general or local acidosis.
H. Herxheimer

Nutrition and Metabolism

1256. The Effect of Malnutrition on the Susceptibility of the Host to Viral Infection

D. H. SPRUNT and C. C. FLANIGAN. *Journal of Experimental Medicine* [J. exp. Med.] 104, 687-706, Nov. 1, 1956. 6 figs., 41 refs.

The old concept that susceptibility to infection is greater in conditions of malnutrition does not always hold true, and at times well-nourished children prove more susceptible than undernourished ones. One of the authors of this paper from the University of Tennessee has previously shown that under certain conditions of starvation the rabbit becomes more resistant to infection with vaccinia. This also holds good for other viruses and species, as has been confirmed by various investigators, and the concept has arisen that any influence inhibitory to host tissue metabolism will also be inhibitory to viral agents. Further experiments have led to the conclusion that the effect of malnutrition on the resistance of an animal is dependent on the state of the animal's nutritional reserves at the time of infection. Thus a well-nourished animal on a poor diet should be at first more susceptible to viral infection, then less susceptible, and finally more susceptible again.

The work now described, which supports this idea, is a study of the effects of progressive long-term dietary depletion on susceptibility to (1) swine influenza in the male CFI mouse and (2) Rous sarcoma virus in the New Hampshire red chicken. Full experimental details are given, including the composition of the low-protein (10%) diet which was eventually chosen as adequate in all respects except for protein and suitable for the maintenance of mice for several months. The susceptibility to virus infection of the animals maintained on this diet was increased during the first 2 to 3 weeks; then followed a period of decreased susceptibility lasting for the next 2 to 3 weeks; and finally after 7 weeks or more on the diet the animals again showed increased susceptibility. The changes in resistance were roughly correlated with the periods of depot fat utilization (decreased susceptibility) and tissue breakdown subsequent to protein starvation (increased susceptibility).

L. A. Elson

1257. Vitamin E Deficiency in Man: Biochemical Evidence in a Patient with Xanthomatous Biliary Cirrhosis

C. W. WOODRUFF. *American Journal of Clinical Nutrition* [Amer. J. clin. Nutr.] 4, 597-602, Nov.-Dec., 1956. 2 figs., 15 refs.

The history is presented of a patient who was first admitted to Vanderbilt University Hospital, Nashville, Tennessee, in 1950, and since that time had been on a fat-free diet. Biochemical examinations recorded at intervals over a 3-year period revealed creatinuria, pentosuria, negligible serum tocopherol levels, very low levels of tocopherol in subcutaneous fat, and increased

susceptibility of erythrocytes to hydrogen peroxide haemolysis. Tocopherol therapy resulted in disappearance of the creatinuria on two occasions and of the pentosuria on one occasion. These findings were interpreted as showing a vitamin-E deficiency; there were also signs of deficient calcium and vitamin-A absorption. A clinical diagnosis of xanthomatous biliary cirrhosis was confirmed post mortem.

F. W. Chattaway

1258. Individual Variations in Expenditure of Energy

J. BOOYENS and R. A. MCCANCE. *Lancet* [Lancet] 1, 225-229, Feb. 2, 1957. 1 fig., 40 refs.

The rate of energy expenditure while lying, sitting, and standing was investigated at the University of Cambridge in 36 healthy subjects (14 males, 22 females). Of these, 6 were selected for a detailed investigation of energy balance for 7 or 14 days, 3 having rates of more than 30% below and one more than 24% above the average of the group; another had a low energy expenditure while lying, normal while sitting, and high while standing. In these 6 subjects energy expenditure was measured during all the more important of their normal occupations.

The results extended and confirmed those of Edholm *et al.* (*Brit. J. Nutr.*, 1955, 9, 286). It was found that the metabolic rates of individuals for basal and similar conditions depart more widely from the average than is usually assumed. This must be considered an important factor in accounting for the differences in energy expenditure between different people leading seemingly similar lives. A small energy expenditure in lying, sitting, and standing need not necessarily result in obesity or an increase in weight. Differences in energy expenditure in active exercise and their variations in lying, sitting, and standing are attributable to differences in degree of training, sense of rhythm, capacity to relax, and tension. The use of triiodothyronine in subjects with a low basal metabolic rate (B.M.R.) and vague symptoms, but no other signs of myxoedema, is discouraged. The experience of the authors and of others suggest that a B.M.R. of 30 to 35% below the average is not necessarily abnormal.

[Many data are presented in tabular form which should be consulted in the original.]

A. Schott

1259. Alkalosis in Sodium and Potassium Depletion (with Especial Reference to Organic Acid Excretion)

B. M. EVANS, I. MACINTYRE, C. R. MACPHERSON, and M. D. MILNE. *Clinical Science* [Clin. Sci.] 16, 53-65, Feb., 1957. 4 figs., 28 refs.

1260. Antilipemic Agent without Anticoagulant Action

E. M. M. BESTERMAN and J. EVANS. *British Medical Journal* [Brit. med. J.] 1, 310-312, Feb. 9, 1957. 5 figs., 9 refs.

Gastroenterology

1261. Cortisone and Ulcerative Colitis. An Adverse Effect

B. N. BROOKE. *Lancet* [*Lancet*] 2, 1175-1177, Dec. 8, 1956. 7 figs., 2 refs.

In this paper from the University of Birmingham the author describes 3 cases of ulcerative colitis coming to operation after treatment with steroids for 6, 5, and 4 weeks respectively had elicited no response. In each case there was gross friability of the wall of the colon with active disintegration leading to peritonitis. All 3 patients died. The author states that "disintegration and adherence have not been observed except in patients treated with cortisone". Attention is drawn to the radiological appearance of "pseudo-haustation" after a barium enema, suggesting that much of the colon is still healthy when in reality the "haustra" are all that remain of the mucosa.

[The abstracter has seen at least one case with such disintegration in which steroid therapy had not been given, and another critically ill patient who had received cortisone for only a few days before laparotomy revealed a similar condition.]

T. D. Kellock

STOMACH AND DUODENUM

1262. Peptic Ulcer: a Follow-up Study after Partial Gastrectomy

J. F. WEIR and H. S. BENNETT. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] 31, 632-639, Nov. 28, 1956.

This is an analysis of 569 cases of peptic ulcer treated at the Mayo Clinic by partial gastrectomy in 1946 and 1947 and followed up for 3 to 4 years. Ten patients (1.8%) died in the immediate postoperative period and 27 subsequently, 4 at least from remote complications of the operation. Recurrent ulcer occurred in 14 cases (3.2%) and dumping of significant degree in 15 (3.4%). This was apparently unrelated to whether the antecolic or retrocolic type of anastomosis was performed and appeared slightly more often after operations for gastric than for duodenal ulcer. The series included only 25 cases in which the Billroth-I operation was performed, in 5 instances for relief of duodenal ulcer, in all of which the result was bad.

It is interesting that among a total of 443 surviving patients about whom adequate data were available, 259 had operations for duodenal ulcer, 117 for gastric ulcer, and 67 for jejunal ulcer.

Guy Blackburn

1263. Complete Nutriment for the Therapy of Peptic Ulcer—Further Studies. Sustagen Therapy of Peptic Ulcer

A. WINKELSTEIN. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] 27, 45-52, Jan., 1957. 4 figs., 9 refs.

1264. Clinical Experience with a Glycine-Calcium Carbonate Mixture. Its Relation to the "Milk Problem" in Peptic Ulcer

A. CORNELL. *Gastroenterology* [*Gastroenterology*] 31, 505-510, Nov., 1956. 8 refs.

After referring to the therapeutic limitations of milk as an antacid, the author describes a clinical trial of a new antacid mixture carried out on 40 private patients with peptic ulceration "who were refractory to ordinary therapy". Of these patients, 34 had duodenal ulcer, 3 had gastric ulcer, and 3 both gastric and duodenal ulcers, confirmed radiologically. All but 10 of the patients were ambulant. Medication was in the form of tablets containing a combination of glycine and calcium carbonate in the proportion 3 : 7, each patient being instructed to take 2 tablets thrice daily after meals and usually 4 tablets on retiring. In addition they had a liberal "ulcer diet" with some antispasmodic-sedative agent before meals. In 32 cases, followed for periods of 8 months to 3 years, "good to excellent" symptomatic relief from ulcer dyspepsia was obtained. The remaining 8 cases were regarded as failures, 4 of them relapsing within 2 to 5 months and the other 4 only after 2 years. There was no toxicity and the patients found the tablets pleasant to take. The author suggests that this mixture affords a valuable means of replacing or supplementing milk as an antacid.

T. J. Thomson

1265. Inhibition of Gastric Emptying and Secretion in Patients with Duodenal Ulcers

J. N. HUNT. *Lancet* [*Lancet*] 1, 132-134, Jan. 19, 1957. 2 figs., 16 refs.

Experiments were carried out at Guy's Hospital, London, to determine how far failure of one of the mechanisms which normally inhibit gastric activity can explain the gastric hyperfunction of patients with duodenal ulcer. Earlier experiments had shown that a test meal containing 100 mEq. of NaCl per litre can be regarded as "a minimal stimulus to the duodenal osmoreceptors whose activity slows gastric emptying", whereas a 10% solution of glucose is a powerful stimulus. In other words, a saline test meal usually emptied more rapidly than plain water, while the glucose solution emptied considerably more slowly, the explanation being that the glucose causes more duodeno-gastric inhibition. In the present study these two test meals (each in a volume of 750 ml.) were given on separate days to 27 healthy student controls and to 16 patients "with a diagnosis of duodenal ulcer without pyloric stenosis under treatment in the medical and surgical wards". The volume left in the stomach was determined at 10 minutes after the saline meal and at 30 minutes after the glucose. Rather less than half the saline meal remained behind, and rather more than half the glucose. [The time intervals were presumably chosen to give a

rough mid-point.] Emptying was about 10% faster in the patients with ulcer, but with the small numbers and wide scatter this difference was not significant. There was no evidence that the duodenal osmoreceptors varied from those in the healthy controls.

[This ingenious experiment, which contradicts widely held views, deserves to be repeated under radiological control and with more orthodox statistical design to reduce variance. Following his usual practice, the author gives the S.D. of the mean, not that from the mean. Rough calculation suggests that the latter would be in the region of ± 40 to 50%—that is, the average emptying rate of 50% is derived from readings scattered fairly evenly from 25% to 75%. Psychological inhibition plays an important part in intubation experiments when emptying is studied over short intervals; students, being at an age when functional disturbances of motility are pronounced, are bad control subjects; and it was presumably found to be impractical to distinguish between the acute phase and the chronic phase of duodenal ulceration.]

Denys Jennings

1266. **Vagal Resection in Treatment of Duodenal Ulcer**
A. A. MACKELVIE. *British Medical Journal* [Brit. med. J.] 1, 321–323, Feb. 9, 1957. 3 refs.

During the period 1947–55, 98% of all cases (473, of which 401 were in men and 72 in women) requiring an interval operation for duodenal ulcer referred to the surgical clinic of the Stirling and Clackmannan Hospitals Group were dealt with by vagotomy. An abdominal approach was used and 5 cm. of each vagus nerve was removed; this was followed by a retrocolic posterior isoperistaltic gastro-jejunostomy, a small stoma being made in the most dependent part of the stomach. In some cases a pyloroplasty was performed in which a diamond-shaped segment of the pylorus was removed. In 2 cases the oesophagus was inadvertently opened and successfully repaired. One patient died of haemorrhage from the inferior phrenic vein during mobilization of the left hepatic lobe. Although 5% of the patients were over 60 and 0.5% over 70 years of age the total mortality was only 2.1%. Two of the 10 deaths were due to paralytic ileus and one to pseudo-membranous enterocolitis 6 days after operation.

Of the 118 patients who underwent vagotomy alone without gastric drainage, 105 were available for follow-up. Of these, 23 had to be treated by gastro-enterostomy for persistent gastric stasis associated with foul flatulence and diarrhoea, and 6 more await this operation. Thus vagal resection alone failed in 29 cases (28%) and this operation is therefore condemned. At these secondary operations the duodenal ulcer was seen to be healed. Of the remaining 76 patients, 3 developed duodenal ulcer and one a gastric ulcer. Many of the rest complain of flatulence and diarrhoea, making this on the whole an unsatisfactory group.

Of the 334 patients subjected to vagotomy and gastro-jejunostomy, of whom 298 were available for a minimum period of follow-up of one year, 238 have no gastric symptoms, 31 only slight symptoms, 8 are much improved, while in 21 the results are poor, 5 having

trouble with "dumping", 3 having marked hypoglycaemic syndromes, and 2 having persisting diarrhoea. In 5 of these cases ulceration has recurred. Vagal crush, which was carried out in 4 cases, was only of temporary benefit.

The author considers that the results of vagotomy with gastro-jejunostomy in these patients compare well with those of gastrectomy.

Norman C. Tanner

1267. **The Role of Gastric Leucopedesis in the Diagnosis of Gastric Disease.** (К вопросу о роли желудочного лейкопедеса в диагностике заболеваний желудка)
N. I. BODROV. *Терапевтический Архив* [Ter. Arkh.] 28, 38–43, No. 8, 1956. 8 refs.

"Gastric leucopedesis" is defined by the author as the number of leucocytes in one cubic millimetre of gastric contents. Normal values are said to vary from 120 to 200 per c.mm., with an average value of 183. Gastric leucopedesis is increased in all conditions associated with inflammatory processes in the gastric mucosa. The present paper reports the results of 103 estimations of gastric leucopedesis performed in 60 patients. The highest values (about 1,130 per c.mm.) were obtained in cases of gastric ulcer, somewhat lower values (around 800 per c.mm.) in gastro-duodenitis and chronic gastritis, and still lower values (624 per c.mm.) in duodenal ulcer. High values were usually obtained in conditions accompanied by achlorhydria and vice versa. A similar inverse relationship was observed between the volume of gastric secretion and the degree of leucopedesis.

It is suggested that repeated estimations of gastric leucopedesis appear to give useful information in the treatment of gastritis. The method used was that of Novikov [but no details of the technique are given]. It is stressed that specimens of the gastric contents for examination must be fresh, in order to avoid false low counts due to destruction of the leucocytes by the gastric juice.

A. Swan

LIVER

1268. **Contribution to the Clinical Study of Pigmentary Cirrhosis.** (Contribution à l'étude clinique de la cirrhose pigmentaire)

M. GIRARD, M. PLAUCHU, J. FAYOLLE, and R. BASTIDE. *Journal de médecine de Lyon* [J. Méd. Lyon] 38, 39–70, Jan. 20, 1957.

This study of pigmentary cirrhosis is based on observations in 31 cases collected during the years 1947–55 in two Lyons hospitals. In most cases there is a clinical picture of cirrhosis occasionally associated with pains in the right hypochondrium or epigastrium. Various dyspeptic manifestations and disturbances of the bowels, sometimes with gastro-intestinal bleeding and icteric or subicteric episodes, appear to be less constant features. Splenomegaly, evidence of collateral circulation, and ascites are rare. Pigmentation of the skin is usually an early sign, but is not always present or may be so slight as to remain unobserved. Diabetes appears rather late and much less frequently than is generally believed (38.7% in the present series). It is usually slight in

degree, but presents difficulties in stabilization with insulin. Sexual disorders were present in less than half of the authors' cases, and consisted mainly in hypogonadism, as shown by a decreased urinary elimination of 17-ketosteroids. Other endocrine disorders are very much less frequent. Cardiovascular involvement resulting in acute heart failure is rare (it occurred in 6.4% in the present series).

The clinical diagnosis is based on the association of hypertrophic cirrhosis with skin pigmentation, while the laboratory diagnosis rests mainly on the finding of a serum iron level above 260 $\mu\text{g.}$ per 100 ml. The results of liver function tests and of blood prothrombin estimation confirm the diagnosis of the cirrhotic process without indicating its pigmentary character. Final confirmation of the diagnosis can be established only by laparoscopy and puncture biopsy of the liver. The histological diagnosis is based on the association of siderosis and sclerosis—true annular cirrhosis plus pigmentation, which is present in every lobule. Steatosis is absent, even in alcoholics.

Pigmentary cirrhosis shows a marked preference for the male sex—30 of the authors' 31 patients were males. The aetiology remains obscure, the most recent theories postulating a disorder of the metabolism of iron, with an increased absorption of alimentary iron at the level of the duodenal mucous membrane. The disease shows a familial and hereditary character, its course is long, and despite treatment it ends fatally. Of the authors' 31 patients, 10 have died, at an average age of 51 years, 6 of them from hepatic causes (3 in hepatic coma, 2 from haematemesis, and one with severe jaundice). Two patients died from acute cardiac failure, one in diabetic coma, and one from uraemia, hypoglycaemia, and terminal hepatic insufficiency. These figures show that, contrary to the usual teaching, patients with pigmentary cirrhosis die more frequently from liver failure than from diabetes.

E. Forrai

1269. Response to Alcohol in Chronic Alcoholics with Liver Disease. Clinical, Pathological, and Metabolic Changes

W. H. J. SUMMERSKILL, S. J. WOLFE, and C. S. DAVIDSON. *Lancet* [Lancet] 1, 335-340, Feb. 16, 1957. 5 figs., 18 refs.

The authors report their observations at the Thorndike Memorial Laboratory, Boston City Hospital, on 7 patients with cirrhosis of the liver associated with chronic alcoholism and malnutrition, 5 also having peripheral neuritis. After a few days' equilibration, the patients were given a diet of some 2,500 Cal. and 90 to 120 ml. of 95% ethyl alcohol daily for 8 days, followed by the diet without alcohol for a further period of 8 days. In 3 cases the diets were kept isocaloric by withdrawal of some carbohydrate during the period of alcohol consumption.

In all the cases the addition of alcohol resulted in gain in weight, improvement in peripheral neuritis, and improved responses to biochemical tests of liver function. There was no evidence that alcohol consumption had any constant or significant effect on

nitrogen balance, and histological examination of liver biopsy specimens did not reveal any deterioration. Weight gain was proportional to caloric intake, and the calories provided as alcohol were adequately utilized for this purpose. Nitrogen retention was proportional to protein intake. The authors state that other effects of administration of alcohol noted were an increased sense of well-being and a "striking" improvement in appetite.

[This is a thorough and well-controlled investigation, but the study periods were short and the results do not mean that alcohol withdrawal has ceased to be a cardinal objective in the long-term management of patients suffering from alcoholic cirrhosis.]

P. C. Reynell

1270. Electrolyte and Circulatory Changes in Terminal Liver Failure

R. HECKER and S. SHERLOCK. *Lancet* [Lancet] 2, 1121-1125, Dec. 1, 1956. 2 figs., 20 refs.

From the Postgraduate Medical School of London (Hammersmith Hospital), the authors describe 9 patients with terminal liver failure due to hepatic cirrhosis or viral hepatitis who had severe hyponatraemia usually associated with uraemia and hypotension. The syndrome was sometimes precipitated or aggravated by paracentesis abdominis. The hyponatraemia could not be corrected by the oral or intravenous administration of sodium chloride, and the urinary sodium excretion remained low. There was evidence of peripheral vasodilatation, and noradrenaline had only a transient effect on the blood pressure. It is suggested that a serum sodium level of less than 130 mEq. per litre in a patient with disease of the liver is a grave prognostic sign.

P. C. Reynell

1271. Chronic (Noncirrhotic) Diffuse Liver Disease. Clinical Studies with Special Reference to Esophageal Varices and Hemorrhage

E. D. PALMER. *American Journal of Digestive Diseases* [Amer. J. dig. Dis.] 1, 499-506, Dec., 1956.

From the Walter Reed Army Hospital, Washington, D.C., the author describes a series of 67 male patients in whom a slight clinical enlargement of the liver was detected, but usually without any hepatic symptoms apart from 11 who had haematemesis and 6 with right upper abdominal pain; 26 of the patients were alcoholics and 23 had had viral hepatitis. Mild splenomegaly was present in 11 patients and spider angiomas were detected in 13. Hepatic biopsy showed portal fibrosis in 24 cases, fatty metamorphosis in 21, portal round-cell infiltration in 4, and a mixture of these features in the remainder. Oesophageal varices were found by means of the Eder-Hufford oesophagoscope in 24 cases, but the finding was confirmed by radiology in only one instance. The author considers that the condition may be a pre-cirrhotic state.

J. McMichael

1272. The Electron Microscopy of Human Liver

D. B. BROWN, C. J. DELOR, M. GREIDER, and W. J. FRAJOLA. *Gastroenterology* [Gastroenterology] 32, 103-118, Jan., 1957. 11 figs., bibliography.

Cardiovascular System

1273. Portacaval Anastomosis

R. M. WALKER. *Lancet [Lancet]* 1, 57-59, Jan. 12, 1957. 3 figs., 3 refs.

In this paper from the University of Bristol the author reports the results in more than 50 patients who have undergone portacaval anastomosis and have survived the operation since 1950. As a result of this experience some fairly definite conclusions as to the indications for the operation have been drawn. The chief is actual haemorrhage or the imminent risk of haemorrhage from oesophageal or gastric varices, the result of extra- or intrahepatic portal obstruction. In ascertaining the site of the obstruction, and whether or not the portal vein was patent, trans-splenic venography was performed in all cases. The state of the portal vein was indicated so clearly by this procedure that the operation was carried out as planned in every case except one. Portacaval anastomosis was not considered advisable if there was evidence of severe liver disease, as indicated by recurrent jaundice, ascites, or very poor results of liver function tests; in no case, also, was the operation performed if the serum albumin level was below 3 g. per 100 ml. By a right thoraco-abdominal approach, usually through the bed of the 9th rib, an end-to-side portacaval anastomosis was carried out in each case.

Out of 56 patients, 53 survived and left hospital. There were only 3 operative deaths, but 5 further patients have died since leaving hospital, 4 from the liver disease, and one from another cause. Only 2 patients had any recurrence of haemorrhage after operation; brief histories of these 2 cases and of the fatal cases are given. The most serious complication of the operation may be recurrent attacks of encephalopathy or coma; this occurred in 9 patients in the present series. Follow-up extending to 5½ years has shown that most of the patients are leading normal lives and are at work.

[This paper must be considered an authoritative statement on the present position regarding portacaval anastomosis in the treatment of portal hypertension.]

F. B. Cockett

1274. Visual Intracardiac Surgery in a Series of One Hundred Eleven Patients

H. SWAN and S. G. BLOUNT. *Journal of the American Medical Association [J. Amer. med. Ass.]* 162, 941-946, Nov. 3, 1956. 7 refs.

This report from the University of Colorado School of Medicine, Denver, summarizes the authors' experience in 111 cases in which open cardiac surgery was performed under general hypothermia. The advantages of operating under direct vision in a dry field are recapitulated, and the belief is expressed that the difficulties and dangers at present associated with the open technique will be overcome with increasing experience. The authors consider the optimum hypothermic temperature is between 29°

and 32° C. (84.2° to 89.6° F.) and that at this temperature the circulation can safely be occluded for 6 minutes, but that occlusion should not exceed 8 minutes. If these limitations are observed they believe that the two greatest dangers—cardiac arrhythmias and disturbances of clotting of the blood—will be largely eliminated. Transfusion of fresh rather than stored blood will also help to prevent the latter complication.

The technique has been restricted to conditions in which the necessary intracardiac manipulations could be completed within 6 to 8 minutes. The conditions and number of cases treated were as follows. (1) Atrial septal defects, 58 cases with 11 deaths. The ostium secundum type of defect is considered to be the ideal condition for closure under hypothermia, and operation is recommended between the ages of 3 and 12 years; of 45 cases of this type good results were obtained in 38, there being 7 deaths. (2) Pulmonary stenosis (all types), 53 cases with 5 deaths (valvular stenosis 25 cases, infundibular stenosis 2, tetralogy and trilogity of Fallot 26); the selection of patients for surgical cure of this lesion is discussed briefly. The repair of ventricular septal defect is considered to be beyond the scope of this technique owing to the complexity and variety of the lesions; among 5 cases in which such repair was attempted there were 4 deaths. On the other hand 3 cases of aortic stenosis were treated with good results; the ideal candidates for this operation are young patients with congenital aortic or subaortic stenosis, or patients under 40 years with rheumatic disease but without calcification of the valve.

Analysis of 19 of the deaths in the series showed that 4 were due to haemorrhage, 4 to postoperative thrombosis, 8 to cardiac failure, and 3 to other causes. Almost all the fatal arrhythmias occurred at temperatures below 28° C., or in connexion with a prolonged period of occlusion. It is considered that with proper selection of cases the mortality from such operations should not exceed 5%.

F. J. Sambrook Gowar

1275. The Precordial Electrocardiogram in Right Ventricular Hypertrophy Due to Mitral Disease. (L'électrocardiogramme précardial d'hypertrophie ventriculaire droite dans la maladie mitrale)

A. BRUSCA, M. D. STAS, V. LEVI, P. F. ANGELINO, and A. A. DATO. *Presse médicale [Presse méd.]* 64, 1989-1991, Nov. 28, 1956. 5 figs., 16 refs.

Of the first 500 patients subjected to mitral valvotomy at the Cardio-surgical Centre of the University of Turin, 406 had pure mitral valvular disease and were divided into three groups: (A) 334 with pure stenosis; (B) 42 with a mitral orifice of less than 1.5 sq. cm., but with significant regurgitation observed by the surgeon before commissurotomy; and (C) 30 with a mitral orifice of more than 1.5 sq. cm. and predominant regurgitation,

The electrocardiogram (ECG) in 143 of these showed the tracing of right ventricular hypertrophy (as defined by the authors) in the precordial leads. This pattern occurred in 134 cases in Group A, 7 in Group B, and 2 in Group C.

On relating the ECG to the size of the mitral orifice it appears that in all Group-A cases with the pattern of right ventricular hypertrophy and in 6 of the 7 cases in Group B the orifice measured less than 1 sq. cm., whereas in the 2 of Group C the orifice was large (2.5 and 3 sq. cm. respectively). On relating the ECG to the data available from cardiac catheterization in 60 cases (53 with pure stenosis, 3 with stenosis and regurgitation, and 4 with predominant regurgitation) it was found that 17 subjects with the pattern of right ventricular hypertrophy had pure and tight stenosis, and the average mean pulmonary arterial pressure in these cases was 64 mm. Hg, whereas in cases without this pattern the average pressure was 38 mm. Hg. Total pulmonary resistance was considerably raised in all cases with the tracing of right ventricular hypertrophy and in 3 cases with significant regurgitation. Pulmonary arteriolar resistance was increased in the cases of right ventricular hypertrophy except for a few with particularly narrow stenosis. But some patients with a normal ECG showed high pulmonary arteriolar resistance, especially if regurgitation was present.

The authors conclude that the cardiographic pattern of right ventricular hypertrophy in the presence of a mitral valvular lesion indicates pure mitral stenosis in 93% of cases and a valvular orifice measuring less than 1 sq. cm. in 98% of cases. But a relatively normal precordial tracing may be found in some cases of tight mitral stenosis even with considerable increase in pulmonary vascular pressure.

R. S. Stevens

1276. Hematologic Observations in Bacterial Endocarditis. Especially the Prevalence of Histiocytes and the Elevation and Variation of the White Cell Count in Blood from the Ear Lobe

G. A. DALAND, L. GOTTLIEB, R. O. WALLERSTEIN, and W. B. CASTLE. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* 48, 827-845, Dec., 1956. 3 figs., 27 refs.

Van Nuys was the first of several observers to point out, in 1907, that histiocytes may be found in the peripheral blood of patients with bacterial endocarditis. The 10 fatal cases of endocarditis reported in the present paper from Boston City Hospital (Harvard Medical School) all showed this phenomenon at some time, and in 2 cases the presence of large numbers of histiocytes in peripheral blood films first suggested the diagnosis.

The leucocyte count in blood from the lobe of the ear was unusually variable, and on the average was 7 times as high as that in blood from the fingertip or antecubital vein; it was found that the corresponding ratio in 10 healthy individuals was 1.3 to 1. The increased count in the 10 patients affected all types of leucocytes, but particularly the histiocytes. It is suggested that the vasculature of the lobe of the ear acts as a filter, whereas that of the fingertip is an ineffective filter

owing to the presence of the numerous arterio-venous anastomoses in that region. In the authors' series the highest count in blood from the ear lobe was 152,000 per c. mm., but a count as high as 700,000 per c.mm. has been reported in bacterial endocarditis. Histiocytes formed up to 41% and monocytes up to 22% of the total leucocyte count, while neutrophil granulocytes showed a shift to the left, and toxic granulation in the later stages; plasma cells were present in 3 cases. There was no correlation between the total leucocyte count or the histiocyte count and the clinical manifestations of bacterial endocarditis. All the 10 patients suffered from a moderately severe progressive anaemia. Examination of aspirated specimens of bone marrow showed granular hyperplasia but no increase in the number of histiocytes or reticulum cells.

T. B. Begg

CONGENITAL HEART DISEASE

1277. Diagnosis of Congenital Aneurysm of the Ventricular Septum during Life

I. STEINBERG. *British Heart Journal [Brit. Heart J.]* 19, 8-12, Jan., 1957. 3 figs., 16 refs.

A case is reported from New York Hospital (Cornell Medical Center), New York, of a woman aged 60 in whom a diagnosis of congenital aneurysm of the ventricular septum was made during life. The patient was admitted for investigation of mild dyspnoea. Clinically, the heart was slightly enlarged, but otherwise normal; the P-R interval was 0.21 second. The diagnosis was made on the finding of a localized bulge in the ventricular septum towards the right ventricle which was observed at angiocardigraphic examination. Up to December, 1955, some 80 cases of congenital aneurysm of the ventricular septum have been reported in the literature, and a case in a boy aged 8 who died in New York Hospital is described and illustrated. The condition is often asymptomatic and is usually found incidentally at necropsy. Commonly, however, it is associated with the occurrence of serious cardiac arrhythmias of unexplained origin.

A. I. Suchett-Kaye

1278. Aneurysms of the Patent Ductus Arteriosus

J. B. DAS and J. T. CHESTERMAN. *Thorax [Thorax]* 11, 295-302, Dec., 1956. 8 figs., 31 refs.

Remarking that in spite of the large number of operations which have been performed for cure of patent ductus arteriosus there are comparatively few reports—56 in the literature since 1827—of aneurysm of this structure, the authors describe, from the City General Hospital, Sheffield, 2 cases which occurred after the ligation of an apparently normal ductus. The first was in a woman aged 26 who presented one year after the original operation with clinical and radiological evidence of recanalization. At a second operation a partly calcified aneurysm of the ductus was resected, with repair of the aorta and pulmonary artery. After a stormy postoperative course the patient made a good recovery. The other case occurred in a 5-year-old girl in whom radiography revealed a large, rounded, hilar

opacity 3 weeks after ligation of an uncomplicated ductus. The mass increased rapidly in size over the next 10 days and was associated with a faint systolic murmur. At operation a thin-walled sac infiltrating the lung was found; this ruptured during dissection, and as a life-saving procedure a hilar tourniquet was applied and the aneurysm removed *en masse* with the left lung. The patient made a good recovery.

A review of the literature showed that congenital aneurysms are rare (2 cases since 1938), as are also those due to dilatation following endarteritis. From the surgeon's point of view the most important are those which follow ligation; these seem to be due to damage caused to the adventitia during dissection and to the use of too tight ligation, with resulting necrosis of the arterial segment. It is suggested that the possibility of aneurysm formation should be borne in mind when there are signs of recanalization, particularly if these are associated with fever, haemoptysis, and hoarseness of recent onset, the last being due to pressure on the recurrent laryngeal nerve. Radiography may reveal a pulsatile or non-pulsatile hilar mass. The sac should be excised, provision being made for adequate control of the great vessels by extensive mobilization of the aorta and intrapericardial clamping of the pulmonary artery if possible. If the lung is involved, pneumonectomy or upper lobectomy may be necessary.

A. M. Macarthur

1279. Patent Ductus Arteriosus. A Follow-up Study of 73 Cases

J. A. COSH. *British Heart Journal* [Brit. Heart J.] 19, 13-22, Jan., 1957. 3 figs., 27 refs.

Of 73 patients with patent ductus arteriosus known to one clinic over the past 30 years, 69 have been traced. Seven have died, of causes that are directly attributable to the ductus in 5 and indirectly in one. Six developed bacterial endocarditis, representing an incidence rate of 0.4% per annum.

The ductus was ligated in 28, the usual indications being dyspnoea, fatigue, poor physique in childhood, cardiac enlargement, or recent bacterial endocarditis. The ductus was not ligated in 34, whose average age is now 26 years. None suffer serious restriction of activity, though 7 are aware of dyspnoea, and 8 have some cardiac enlargement. In 4 the continuous murmur has disappeared. Twenty-one of the 35 patients with a thrill, and only 5 of the 24 without a thrill, were selected for operation. Childbirth occurred 23 times in patients with the ductus patent, without difficulty or complication. Only one patient required termination of pregnancy with sterilization. Children with patent ductus were significantly under-weight when compared with normal controls. Only 4 out of 13 showed a significant improvement in weight in the years following ligation of the ductus.—[Author's summary.]

1280. Oxygen Administration in Differential Diagnosis in Cyanotic Patients

L. BROTMACHER. *Guy's Hospital Reports* [Guy's Hosp. Rep.] 106, 29-35, 1957. 14 refs.

CHRONIC VALVULAR DISEASE

1281. Aortic Stenosis and the So-called Rheumatic Valvular Diseases in a Postmortem Material. [In English] C. MÜLLER. *Acta medica Scandinavica* [Acta med. scand.] 156, 241-261, Dec. 31, 1956. 25 refs.

An analysis is presented of 509 cases of so-called rheumatic (cicatricial) valvular heart disease found at necropsy on 8,663 patients in Ullevål Hospital, Oslo, two 5-year periods being covered, 1923-7 with 3,336 necropsies and 1943-7 with 5,327 necropsies. The incidence and location of the lesions were about the same in each period. There were 177 cases (34.8%) of isolated aortic stenosis, 155 (30.5%) of isolated mitral stenosis, 113 (22.2%) of combined mitral and aortic disease, 45 (8.8%) of isolated mitral incompetence, and 19 (3.7%) of isolated aortic incompetence. The average age at death was very high; it was lowest in patients with isolated mitral stenosis (but even here it was over 60 years) and highest in those with isolated aortic stenosis (72 years). Statistically adjusted, the sex distribution showed an over-all preponderance of females, although most of the cases of aortic lesions were in males. Myocardial infarction was present in 12.3% of the cases and was commoner in aortic than in mitral disease. Even in patients with aortic stenosis, atheroma of the aorta was a very frequent finding.

The aetiology of this valvular condition is briefly discussed and its frequent association with atherosclerosis of the valves is mentioned.

[The figures are based on macroscopic findings only and therefore the true incidence of rheumatic lesions is uncertain.] A. Wynn Williams

1282. Mitral Regurgitation with Mobile Valve Cusps

D. M. DOUGLAS. *British Medical Journal* [Brit. med. J.] 1, 191-192, Jan. 26, 1957. 2 figs., 6 refs.

In the assessment of the suitability of patients for the operation of mitral valvotomy a loud, abrupt first sound is generally taken as evidence of the presence of pure mitral stenosis. In this condition the cusps of the mitral valve are fused but pliable, whereas in mitral regurgitation the cusps are rigid and contracted. The author points out, however, that the abrupt first heart sound in mitral disease may be a sign of cusp mobility rather than of stenosis, and that mitral regurgitation may occur although the cusps are soft and mobile.

It is true that this state of affairs is uncommon, but in this communication from the University of St. Andrews the case histories of three patients are presented in whom a diagnosis of mitral stenosis was made on the basis of clinical findings, but in whom at operation significant regurgitation in the presence of mobile valve cusps was found. These cases, which occurred in 3 women aged 30, 32, and 37, were seen in a series of 183 patients undergoing valvotomy. Since the impression was also formed at operation that the chordae tendineae were shortened, the author suggests that regurgitation in these cases may be due to fixation of the cusps by shortened chordae, the actual damage to

the cusps themselves being minimal. He considers that the basis of the opening snap in mitral valve disease may also be related more accurately to mobility than to stenosis of the valve.

F. Storer

DISTURBANCES OF RHYTHM AND CONDUCTION

1283. Effects of Intravenous Digoxin in Uncontrolled Auricular Fibrillation

J. HAMMOND and W. WHITAKER. *British Heart Journal* [Brit. Heart J.] 19, 23-33, Jan., 1957. 2 figs., 44 refs.

Changes in systemic and renal circulations and salt excretion following a single intravenous injection of digoxin were studied in 13 patients with uncontrolled auricular fibrillation, of whom 6 had congestive heart failure. The heart rate decreased in all 13 patients. The cardiac output increased in 4 patients with congestive heart failure, was unchanged in one, and decreased in the other. Much smaller changes occurred in those without heart failure. In most patients there was an initial rise in systolic blood pressure and, less consistently, in diastolic pressure. The subsequent changes were variable, but the systolic pressure usually remained raised while there was little change in the diastolic pressure.

In 5 patients with heart failure the right atrial pressure decreased and in the other it remained unchanged. Only one patient without heart failure showed much fall in right atrial pressure and she had an unusually high initial level.

Before digoxin all 13 patients had abnormally low renal blood flows and renal plasma flows and all but one patient, without heart failure, had low glomerular filtration rates. The smallest values were seen in those with heart failure. After digoxin there was an increase in renal blood flow, renal plasma flow, and glomerular filtration rate in 3 of 4 patients with heart failure who showed an increase in cardiac output. In 2 without heart failure there was an increase in renal blood flow and renal plasma flow which was independent of an increase in cardiac output and was unaccompanied by a similar change in glomerular filtration rate. In the other 8 there was little or no change in renal circulation. In most patients changes in renal plasma flow and glomerular filtration rate were unaccompanied by alterations in filtration fractions, which remained abnormally high.

The systemic vascular resistance fell in all except one patient with congestive heart failure, but no consistent changes occurred in those without heart failure. Digoxin did not appear to have any direct effect on peripheral vascular resistance since the changes observed in those with heart failure were probably due to a reflex baroreceptor response. There were no uniform changes in the renal vascular resistance. Although the renal fraction of the cardiac output was initially abnormally low in most patients, digoxin produced no consistent change in this fraction, and appeared to have no immediate effect in restoring a normal distribution of blood to the kidneys.

There was a large increase in salt excretion in all 3 patients with congestive heart failure who showed a rise in cardiac output, renal blood flow, renal plasma flow, and glomerular filtration rate. This increase in salt excretion was probably caused by an improvement in renal circulation following the rise in cardiac output. There was, however, an increase in salt excretion in some others where there was no evidence of a change in the tubular load, suggesting that digoxin also had a direct effect on tubular reabsorption of salt.—[Authors' summary.]

1284. Experiences with Pulsus Alternans: Ventricular Alternation and the Stage of Heart Failure

J. M. RYAN, J. F. SCHIEVE, H. B. HULL, and B. M. OSER. *Circulation* [Circulation (N.Y.)] 14, 1099-1103, Dec., 1956. 5 figs., 6 refs.

Pulsus alternans, which apparently does not develop in the absence of organic heart disease, may not have the serious prognostic importance usually ascribed to it. In a study at the Ohio State University College of Medicine, Columbus, it was noted that in patients with myocardial insufficiency but not in cardiac failure pulsus alternans occurred in response to exercise. Sustained pulsus alternans at rest was found in patients who were or had been in cardiac failure, and this type was exaggerated by application of a venous tourniquet and diminished by exercise. Prognosis in these cases depends on the degree of failure, and indeed, pulsus alternans in such patients may disappear as cardiac failure advances.

T. Semple

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1285. Long Term Prognosis of Myocardial Infarction. Analysis in Relation to Russek's Classification of "Good" and "Poor" Risk Cases. [In English]

O. C. OLSEN, T. KAHRS, O. RØMCKE, and P. LINGJAERDE. *Acta medica Scandinavica* [Acta med. scand.] 156, Suppl. 319, 17-26, 1956. 17 refs.

In this study from the Drammen Hospital, Norway, an attempt has been made to determine whether Russek's classification of cases of myocardial infarction into "good-risk" and "poor-risk" groups (*J. Amer. med. Ass.*, 1954, 156, 765; *Abstracts of World Medicine*, 1955, 17, 379) is of value in deciding the desirability of long-term anticoagulant therapy. The material consisted of 306 cases admitted to hospital with myocardial infarction between 1936 and 1951, of which 67 were excluded from the study for various reasons. Of the 239 remaining, 113 died in hospital or within 2 months and 126 were available for follow-up. Of these, 81 were men and 45 women, and at the end of the study 87 had died and 39 were still alive. None received anticoagulants after discharge from hospital. Of the 58 dying within 5 years, 34 were "good-risk" and 24 "poor-risk" cases. Of the 46 who survived from 5 to 10 years, 33 were in the "good-risk" group, whereas only 3 of the 22 surviving over 10 years were "poor-

risk" cases. However, over one-half of the deaths in the "good-risk" group (31 out of 54) were due, or probably due, to a fresh infarction.

It is therefore concluded that while the average survival in "good-risk" cases is longer than in "poor-risk" cases, both groups equally need long-term anticoagulant therapy to prevent further myocardial infarction.

C. Bruce Perry

1286. **Trial of Drugs for Angina of Effort: the Oral Use of Dihydroxypropyltheophylline and Aminophylline**
R. FIFE, G. HOWITT, and J. R. ROY. *Scottish Medical Journal* [Scot. med. J.] 2, 11-16, Jan., 1957. 28 refs.

A controlled trial of dihydroxypropyltheophylline (DHT) and aminophylline given by mouth in the treatment of angina of effort is reported from the Royal Infirmary, Glasgow. Of 104 patients originally selected, 81 completed the trial, which consisted in taking each of the following in tablet form 3 times a day after meals for a fortnight: aminophylline, 0.1 g.; aminophylline, 0.2 g.; DHT, 0.222 g.; and a placebo. The double-blind technique was used; the patients were unaware that one batch of tablets was inert and neither they nor their doctor knew the identity of the preparations. The patients recorded the frequency and severity of attacks of pain while taking the drugs and the placebo, the number of tablets of glyceryl trinitrate used, and any symptoms attributable to the trial tablets, these observations being assessed fortnightly. In the dosages employed no significant difference was observed between the drugs in their effect on angina of effort; moreover, the placebo appeared to be as effective as the drugs. There were, however, fewer side-effects of the dyspeptic type with DHT than with aminophylline.

G. S. Crockett

1287. **Treatment of Angina Pectoris with Disodium Ethylene Diamine Tetraacetic Acid**

N. E. CLARKE, C. N. CLARKE, and R. E. MOSHER. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 232, 654-666, Dec., 1956. 2 figs., 20 refs.

The purpose of this investigation, reported from the Providence Hospital, Detroit, was to ascertain the clinical effect of a chelating agent, disodium ethylenediamine tetraacetic acid (disodium edetate) on patients with angina pectoris. This agent is known to be effective in safely removing metastatic calcium in renal calcinosis, and the authors hoped that it might be equally successful in disintegrating the calcium-containing organic matrix of atheromatous plaques.

Twenty patients with angina pectoris were studied, 7 with evidence of previous myocardial infarction. Infusions of 5 g. of disodium edetate in 500 ml. of 5% glucose or normal saline solution were given intravenously up to a total of between 15 and 60, these being administered either daily or on alternate days with suitable rest periods. The authors describe 2 cases, not included in this series, in which remarkable mobilization of metastatic calcium deposits occurred after treatment with disodium edetate. Of the 20 cases of angina described, the authors consider that 19 obtained relief

of symptoms with treatment and that in 6 out of 14 patients with abnormal electrocardiograms reversion to normal occurred. One patient died shortly after an infusion of disodium edetate, possibly from lodgement of a calcium embolus in the brain (only a limited post-mortem examination was performed).

Possible theoretical biochemical actions of disodium edetate and the evidence in support of an intimate relationship between calcium and cholesterol in the atheromatous matrix are discussed.

[The abstracter considers that comparable improvement to that seen in some of these cases may occur with little or no specific treatment.]

Francis Page

HEART FAILURE

1288. **Tricuspid Incompetence and Right Ventricular Output in Congestive Heart Failure**

P. KORNER and J. SHILLINGFORD. *British Heart Journal* [Brit. Heart J.] 19, 1-7, Jan., 1957. 6 figs., 8 refs.

At Hammersmith Hospital (Postgraduate Medical School of London) 14 patients in congestive cardiac failure and with clinical signs of tricuspid valvular incompetence were studied with a view to determining quantitatively the amount of regurgitation through the incompetent tricuspid valves, the method of estimation of the regurgitant flow being that employing the dye dilution technique as previously described by the authors (*Clin. Sci.*, 1955, 14, 553). The results were correlated with the clinical and, in some cases, the necropsy findings, and are discussed in relation to the performance of the right ventricle in congestive cardiac failure.

Generally in these patients the total right ventricular output remained high and relatively fixed. After mild exertion the slight increase in right ventricular output was due to an increase in backward flow, the forward cardiac output remaining the same or diminishing. Rest had the opposite effect, increasing the efficiency of performance of the right ventricle by decreasing the regurgitant flow into the right auricle.

A. I. Suchett-Kaye

1289. **The Treatment of Acute Pulmonary Oedema with Chlorpromazine.** (Traitement de l'œdème aigu du poumon par la chlorpromazine)

R. LACASSIE. *Presse médicale* [Presse méd.] 64, 1837-1839, Nov. 7, 1956. 16 refs.

Acute pulmonary oedema is usually treated by administration of morphine and occasionally by venesection, and to prevent attacks a low-salt diet, mercurial diuretics, and aminophylline are commonly given prophylactically. The present author, on the basis of 3 cases treated with chlorpromazine, claims that this drug is equally effective in treatment. For the acute attack associated with systemic hypertension chlorpromazine in a dilution of 1 in 10 is given by slow intravenous infusion. As a measure of prophylaxis an intramuscular injection of the drug is given at night, in addition to administration of a low-sodium diet and occasional injection of a mercurial diuretic. Clinical details of the

3 cases are presented and other forms of treatment of acute pulmonary oedema as described in the literature are discussed.

James W. Brown

BLOOD VESSELS

1290. **Statistical Analysis of the Results of Penicillin Therapy on the Effects of Syphilitic Aortitis.** (Análisis estadístico del resultado del tratamiento con penicilina de la insuficiencia aortica sifilítica)

E. VIVAS SALAS. *Archivos del Instituto de cardiología de México [Arch. Inst. Cardiol. Méx.]* 26, 435-448, July-Aug., 1956 [received Jan., 1957]. 1 fig., 30 refs.

The author presents, from the National Institute of Venereology, Caracas, Venezuela, the results of a careful study of 114 patients, 87 men and 27 women, with syphilitic aortic insufficiency who were treated with 10 mega units of penicillin given by intramuscular injection during 17 days and observed for an average period of 13.3 months. It is mentioned that among 756 patients with cardiovascular syphilis who have been treated with penicillin no case of Herxheimer reaction or of therapeutic paradox has occurred.

The results of studies of functional capacity, circulation time, heart size, intensity of the diastolic murmur, and of quantitative Kahn tests are tabulated separately for two groups of patients, those aged 20 to 39 years and those aged 40 years and over. Functional capacity was improved in both groups and the diminution in the strength of the Kahn reaction was statistically significant in the younger group. Arm-to-lung circulation time showed improvement in both groups, but the arm-to-tongue circulation time was unaffected by treatment, as was also the transverse diameter of the heart and the intensity of the early diastolic murmur. Among the patients studied were 4 pregnant women, all of whom had normal deliveries.

[The follow-up period is short, but the author sets out clearly the good results that can be obtained from treatment with penicillin. However, the question of how much of the improvement can be attributed to general medical care cannot be answered.]

Eric Dunlop

1291. **Nicotinyl Alcohol Tartrate in Intermittent Claudication**

R. O. GILLHESPY. *British Medical Journal [Brit. med. J.]* 1, 207-208, Jan. 26, 1957. 10 refs.

Nicotinyl alcohol tartrate is a long-acting vasodilator with an action mainly on small arteries and arterioles. In a controlled "blind" study of its value in the treatment of intermittent claudication in which 50 patients with this complaint attending the Dudley Road Hospital, Birmingham, took part, half were given 25 mg. of nicotinyl alcohol tartrate four times daily and the other half dummy tablets, the author being unaware of the identity of the tablets until the end of trial, which lasted about 2½ years. The criteria for inclusion in the trial were that patients had to have typical intermittent claudication, absence of pulsation in a limb, and evidence of trophic changes in the skin. During the course of the

trial 15 patients died and 5 others were lost for various reasons. Each patient was treated for at least 18 months and no significant side-effects were observed. Judgment of progress depended mainly on increase in the distance walked before claudication appeared, as reported by the patient himself, the author having found this to be a reliable measure of change.

The final results showed that of the 17 patients receiving the drug 10 reported moderate improvement, 3 slight improvement, and 4 no benefit; of the 13 given the placebo the corresponding figures were 0, 4, and 9. The author concludes that nicotinyl alcohol tartrate is a useful drug in the treatment of intermittent claudication, particularly when the progressive nature of the disease is kept in mind.

F. Starer

HYPERTENSION

1292. **Renal Factors in the Pathogenesis of Hypertension.** (О роли почечного фактора в патогенезе гипертонической болезни)

M. Y. RATNER. *Терапевтический Архив [Ter. Arkh.]* 28, 9-18, No. 8, 1956. 4 figs., 33 refs.

The author holds that the production of renin by the kidneys is predominantly under the control of the nervous system. Essential hypertension is then regarded as a neurological disorder, and hypertension due to renal ischaemia (Goldblatt kidney) as a clinically rare form of stimulation of the renin-producing mechanism.

Numerous findings based on the author's own experiments and on those of other (mostly Russian) workers are quoted in support of his views. They can be listed as follows. (1) Lack of correlation between the height of the blood pressure and the renal blood flow was confirmed by the author in 208 cases of essential hypertension. (2) Reduction of blood pressure in hypertensive patients induced by barbiturates was usually found to be accompanied by a further fall in the renal blood flow. (3) A hypertensive reaction induced by "phenamin" was not usually followed by any change in the renal blood flow, and in a few cases was even followed by its increase. (4) In patients with essential hypertension denervation of the kidneys is known to lead to a prolonged fall in the blood pressure. (5) In rabbits a form of hypertension induced by the division of both pairs of the depressor nerves (the aortic and the carotid), which the author calls "experimental neurogenic hypertension", was invariably abolished by severing the nerve supply of the kidneys, and the blood pressure remained at normal level for a period of 22 to 25 days, until "re-innervation became established". Conversely, after preliminary renal denervation such experimental neurogenic hypertension in rabbits could not be induced. (6) Estimations of the amount of renin in the kidneys of these rabbits revealed a significant rise, even during the first few days of the experimental neurogenic hypertension, that is, while the renal blood flow remained normal. But after renal denervation the content of renin in the kidneys fell, sometimes to levels too low to be estimated.

In addition to these findings the author postulates the existence of some other pressor factor which is responsible for hypertension in conditions associated with the destruction of renal parenchyma, when, as has been experimentally established, renin disappears. Such a state of affairs exists in malignant hypertension, after complete occlusion of the renal arteries as in Goldblatt's experiment, and in animals subjected to experimental bilateral nephrectomy and subsequently kept alive by means of an artificial kidney.

A. Swan

1293. Hypnotherapy in Hypertensive Disease. Treatment by Means of Hypnotic Sleep of Patients with Hypertensive Disease. (Лечение гипнотическим сном больных гипертонической болезнью)

A. S. SMETNEV. *Терапевтический Архив* [Ter. Arkh.] 28, 18-26, No. 8, 1956. 2 figs.

The author accepts as an established fact the theory that hypertension is a form of neurosis which depends upon the formation and perpetuation, in the subcortical centres, of a focus of irritation affecting the vasomotor regulating mechanism.

Hypnotic suggestion, followed by a period of sleep which was gradually increased from 2 hours to 12 hours daily, was employed in the treatment of 118 hypertensive patients in whom the average duration of the disease was 4½ years and the arterial blood pressure ranged from 140/80 to 240/170 mm. Hg. The hypnotherapy was preceded by a preliminary period of rest of 7 to 10 days.

In 79 of the 118 cases the blood pressure fell after the course of hypnotic treatment [of unspecified duration] to normal limits. Subjective improvement was reported by the great majority of patients, and in 63 cases the symptoms of hypertension disappeared. Of 50 cases which were followed up for 3 years, improvement lasting up to 12 months was found in 35 and for 1 to 3 years in 14 cases. Capillaroscopy and chronaximetry were also employed to provide objective criteria of improvement. The former showed some return to normal of the condition of the arterioles and venules in cases of early, mild hypertension, and the latter demonstrated a great increase in chronaxy, at least during the period of hypnotic sleep, from the abnormally low values usual in hypertensive subjects. In most of these cases only light hypnosis (1st stage) was used.

A. Swan

1294. Adrenaline Sensitivity of Peripheral Blood Vessels in Human Hypertension

R. S. DUFF. *British Heart Journal* [Brit. Heart J.] 19, 45-52, Jan., 1957. 5 figs., 14 refs.

In this paper from St. Bartholomew's Hospital, London, the author describes a method of measuring the sensitivity to adrenaline of the blood vessels of the hand, the blood flow in both hands being determined simultaneously by venous occlusion plethysmography. A solution of adrenaline was infused into the brachial artery of the test hand, and each subject was tested with 2 or 3 different concentrations, giving rates of 1/64, 1/16, and 1/8 µg. per minute. During a control period the variations in blood flow to the two hands were

found to be similar in degree; the vasoconstriction caused by the adrenaline could therefore be determined by comparing the change in the level of blood flow in the test hand with that in the control hand.

In a group of 25 patients with hypertension the degree of constriction caused by adrenaline was almost three times as great as that observed in a group of 39 subjects with normal blood pressure. In one-third of the hypertensive patients the vascular sensitivity was not outside the normal range, but in the others it increased with the severity of the hypertensive process. It is suggested that further study of these two groups of hypertensive patients may lead to a closer understanding of the mechanism of hypertension.

H. E. Holling

1295. Acute and Chronic Cardiovascular Effects of Pentolinium in Hypertensive Patients

J. R. SMITH and S. W. HOOBLER. *Circulation* [Circulation (N.Y.)] 14, 1061-1068, Dec., 1956. 2 figs., 25 refs.

The effect of pentolinium on the cardiac output and peripheral resistance in hypertension was studied at the University of Michigan Medical School, Ann Arbor, cardiac output being determined serially in ambulatory patients by means of a dye-dilution technique with radioactive iodinated serum albumin as the "dye". With the patient in the sitting position cardiac output was determined before and after intravenous infusion of pentolinium and later after prolonged oral administration of the drug. It was found that reduction in blood pressure was accompanied by a parallel fall in the cardiac index and stroke volume, while the calculated peripheral resistance remained essentially unchanged. After intravenous infusion of pentolinium the pulmonary blood volume fell on the average by over 20%.

These observations suggest that ganglionic blockade does not reduce arteriolar tone but acts upon cardiac output through a reduction in venous return to the heart, perhaps by reducing the peripheral-to-central venous pressure gradient.

T. Semple

1296. A Comparison between Protoveratrine A and Protoveratrine B Orally in Arterial Hypertension; a Therapeutically Important Difference in Activity

B. M. WINER. *New England Journal of Medicine* [New Engl. J. Med.] 255, 1173-1179, Dec. 20, 1956. 5 figs., 25 refs.

The limiting factor in the clinical use of the veratrum alkaloids has been the narrow dosage range between hypotensive action and emetic side-effects, especially when given by mouth. The expectation that protoveratrine, thought to be a pure alkaloid derivative of veratrum, would be less liable to produce emesis in an effective oral dose has not been fulfilled. However, it has been shown that protoveratrine is composed of two alkaloids, protoveratrine A and B, the pharmacological differences between them being considered to be small and of little clinical significance. In this paper from Beth Israel Hospital and Harvard Medical School, Boston, a comparative study of the efficacy of these two alkaloids when given by mouth to 13 patients with sustained hypertension is reported; it had previously

been observed that they were of equal hypotensive potency when given intravenously.

Protoveratrine A proved to be effectively hypotensive, the action starting in 45 to 90 minutes and lasting 4 to 6 hours. The dosage was 0.3 to 0.5 mg. daily, which was increased gradually until a marked fall in blood pressure or vomiting prohibited any further increase. In all except one of the patients the blood pressure was lowered by the correct dosage without nausea or vomiting. Protoveratrine B in a dosage of 1.5 to 2 mg. daily had no effect on the blood pressure, but in the dose range 4.0 to 7.5 mg. daily there was a striking reduction in blood pressure 2 to 3 hours after administration of the drug, with a return to the previous level within 6 hours. With the large doses nausea and vomiting were not observed, but in a few instances there were effects on muscle function resembling clinical myotonic syndromes.

These results are considered to provide definite evidence of the value of using single pure alkaloids rather than a mixture for administration by mouth. In the author's view further investigation of pure veratrum alkaloids is indicated.

P. Hugh-Jones

PULMONARY CIRCULATION

1297. Clinical, Physiological, and Pathological Considerations in Patients with Idiopathic Pulmonary Hypertension

J. T. SHEPHERD, J. E. EDWARDS, H. B. BURCHELL, H. J. C. SWAN, and E. H. WOOD. *British Heart Journal* [Brit. Heart J.] 19, 70-82, Jan., 1957. 4 figs., 24 refs.

This report concerns 10 patients in whom a diagnosis of idiopathic pulmonary hypertension was made on the basis of clinical and physiological studies. Such a diagnosis is chiefly a process of elimination of other types of heart disease of which pulmonary hypertension is a functional accompaniment. The certain differentiation can be made from the great majority of such conditions by the critical application of certain physiological techniques, notably the indicator-dilution method. The only intracardiac shunt consistent with a diagnosis of idiopathic pulmonary hypertension is a veno-arterial shunt through a valve-competent patent foramen ovale. By definition, pulmonary hypertension associated with a true atrial septal defect is not of the idiopathic type. However, the certain differentiation by clinical or physiological methods of a veno-arterial shunt occurring via an unsealed valve-competent foramen ovale or via a true atrial septal defect may be impossible, as attested by one case in the present series.

Post-mortem studies were carried out on the 3 patients who died. In one, the only man in the series, a true atrial septal defect was found, but the appearance of the heart did not suggest that a large left-to-right shunt had ever been present. The histological appearance of the small pulmonary arteries was varied, but examination of serial sections along the course of a vessel often revealed localized obstructions, which were frequently seen in vessels, the lumina of which were unobstructed throughout most of their length. In the patients studied

post mortem the organic changes in the pulmonary vessels appeared sufficient to account for the pulmonary hypertension.—[From the authors' summary.]

1298. Idiopathic Pulmonary Hypertension

D. HEATH, W. WHITAKER, and J. W. BROWN. *British Heart Journal* [Brit. Heart J.] 19, 83-92, Jan., 1957. 5 figs., 25 refs.

The authors describe 4 cases of idiopathic pulmonary hypertension in all of which the classic signs of pulmonary hypertension and of congestive cardiac failure were present. The diagnosis was established by cardiac catheterization—the only method which excludes intracardiac shunt as a cause of the hypertension. At necropsy in 3 of the cases the pulmonary arterioles showed intimal fibrosis and the presence of a distinct muscular media. The "muscular" pulmonary arteries showed medial necrosis, intimal fibrosis, and occlusion of the lumen. The authors point out that with the exception of arterial necrosis, these lesions also occur in severe pulmonary hypertension secondary to other conditions.

Bernard Isaacs

1299. Solitary Pulmonary Hypertension

W. EVANS, D. S. SHORT, and D. E. BEDFORD. *British Heart Journal* [Brit. Heart J.] 19, 93-116, Jan., 1957. 23 figs., 36 refs.

In this paper from the London, Middlesex, and National Heart Hospitals, London, the findings in 11 cases in which pulmonary hypertension was present without any obvious cause are described. All the patients (females aged 7 to 64 years) died, and at necropsy the pulmonary vasculature was specially studied by histological and arteriographic techniques. The main pathological findings in 9 cases were thrombotic occlusion of one or more of the segmental branches of the pulmonary artery, abnormal bronchopulmonary anastomoses, proliferation of the intima and thrombosis of the muscular arteries and arterioles, and areas of hypoplasia and aplasia of the media of the "muscular" arteries. In one case in which vascular obstruction was absent on histological examination, arteriography showed generalized constriction of the lesser pulmonary arteries. Discussing the question whether these arterial lesions caused, or were caused by, pulmonary hypertension, the authors point out that the pathological changes in their patients were ample to account for maintenance of hypertension. In their view the finding that medial hypoplasia and aplasia often occurred in solitary pulmonary hypertension suggests that these medial defects were an intimal reaction to normal fluctuations in pulmonary arterial pressure, and in this way initiated hypertension.

[The original paper should be studied for the detailed clinical and pathological data and for the excellent illustrations.]

Bernard Isaacs

1300. Primary Pulmonary Hypertension. Review of Literature and Results of Cardiac Catheterization in Ten Patients

D. W. CHAPMAN, J. P. ABBOTT, and J. LATSON. *Circulation* [Circulation (N.Y.)] 15, 35-46, Jan., 1957. 4 figs., 20 refs.

Haematology

1301. The Crisis in Sickle Cell Anemia. Hematologic Studies

L. W. DIGGS. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] 26, 1109-1118, Oct., 1956. 6 figs., 17 refs.

Clinical and haematological studies were carried out on 166 patients with sickle-cell anaemia who were admitted to the City of Memphis Hospital, Tennessee, on 747 occasions suffering from clinical crises, further detailed investigations of the fluctuation of various haematological values in 30 of the patients also being performed between crises. In no case was there any evidence of an increase in the degree of anaemia during a crisis; the absence during these episodes of any significant alteration in the reticulocyte, erythrocyte, and nucleated erythrocyte counts and in the faecal urobilinogen content indicated that the rate of haemolysis was unchanged. In only one case was an aplastic crisis observed. A few of the patients showed a very high reticulocyte count and a hypercellular marrow, but this was followed by a gradual return to normal values without any change in the level of the serum bilirubin; it is suggested that these patients were recovering from an aplastic crisis.

The author concludes that there is no evidence to support the belief that haemolytic crises occur in the course of sickle-cell anaemia. Clinical crises are probably due to occlusive vascular complications, but the degree of haemolysis remains virtually unchanged during the lifetime of the patient.

J. L. Markson

1302. Sickle-cell-Thalassaemia Disease in South Turkey

M. AKSOY and H. LEHMANN. *British Medical Journal* [Brit. med. J.] 1, 734-738, March 30, 1957. 1 fig., 30 refs.

1303. A Laboratory Study of the Carrier State in Classic Haemophilia

A. MARGOLIUS and O. D. RATNOFF. *Journal of Clinical Investigation* [J. clin. Invest.] 35, 1316-1323, Nov., 1956. 1 fig., bibliography.

It can be assumed on genetic grounds that three groups of individuals are carriers of the haemorrhagic disorder in haemophilia, namely, all the daughters of a haemophiliac, the mother of 2 or more haemophilic sons, and the mother of a single haemophiliac if she has other haemophilic relatives. There is a 50% chance that the daughters of a transmitter female will in turn be carriers and this paper from the Western Reserve University School of Medicine, Cleveland, Ohio, describes an investigation into the coagulation system of 27 such individuals belonging to 18 families in which classic haemophilia was confirmed in at least one affected male.

The techniques used were the whole-blood coagulation time in glass coated with silicone, a prothrombin

consumption technique, and assays of antihaemophilic globulin. The antihaemophilic activity was measured by the ability of test and control plasmas (treated with an adsorbing precipitate) to correct the recalcification of known haemophilic plasma. The thromboplastin-generation technique was also employed. Of the 19 presumptive and 8 possible carriers studied, only one showed a significant reduction in antihaemophilic globulin activity; she also had a prolonged blood clotting time. It is of interest that this girl belonged to a family in which the defect in the affected males was relatively mild.

[The paper includes an admirable review of the literature relevant to this problem.] A. S. Douglas

1304 (a). The Hemostatic Defect of Uremia. I. Clinical Investigation of Three Patients with Acute Post-traumatic Renal Insufficiency

C. LARRAIN and E. ADELSON. *Blood* [Blood] 11, 1059-1066, Dec., 1956. 28 refs.

1304 (b). The Hemostatic Defect of Uremia. II. Investigation of Dogs with Experimentally Produced Acute Urinary Retention

C. LARRAIN and R. D. LANGDELL. *Blood* [Blood] 11, 1067-1072, Dec., 1956. 11 refs.

These two papers describe investigations carried out at the Walter Reed Army Medical Center, Washington, D.C., into the haemostatic mechanism concerned in acute renal failure.

The first paper reports studies performed on 3 patients with acute renal damage, in one case following ingestion of "bootleg alcohol and cigaret-lighter fluid", and in the other 2 as a sequel to traumatic injury. All three patients developed a significant haemorrhagic tendency. A complete study of the vascular and coagulation components of the haemostatic mechanism was made. [For details of the techniques used the original paper should be studied.] The significant findings in all 3 cases were a prolonged bleeding time and prolongation of the whole-blood coagulation time in silicone, and in 2 of the cases defective prothrombin consumption. No final explanation for the failure to utilize prothrombin at the normal rate was found; there was no deficiency of plasma thromboplastin components, no marked depression of the platelet count, and no circulating thromboplastin inhibitors.

The second paper describes a related study on dogs in which acute urinary retention was produced by ligation of the ureters and the haemostatic mechanism studied as uraemia developed. In contrast to the human subjects prolongation of the bleeding time was not seen nor clinical evidence of abnormal haemorrhage. There was, however, as in the patients, prolongation of the whole-blood clotting time in silicone.

A. S. Douglas

Respiratory System

1305. Investigation of Idiopathic Pleural Effusions by Thoracoscopy

S. J. FLEISHMAN, A. I. LICHTER, G. BUCHANAN, and R. J. S. SICHEL. *Thorax* [Thorax] 11, 324-327, Dec., 1956. 1 fig., 5 refs.

This report from the South African Institute of Medical Research, Johannesburg, describes the thoracoscopic findings in 76 African gold-mine workers suffering from "idiopathic" pleural effusion. The patients were drawn from a wide area so that follow-up examinations were not practicable, and their clinical histories were often unsatisfactory; a reliable method of establishing the aetiology of the effusions was therefore desirable. It was found that in most cases the pleura was covered by a layer of fibrin and adhesions were frequent; tubercles were rarely seen, and the thoracoscopic appearances in themselves could not be relied on in attempting to determine the cause of the effusion. Biopsy specimens of the pleura were therefore taken in all but 5 of the cases, stained for tubercle bacilli, and examined histologically, and special preparations were also inoculated into guinea-pigs and on Löwenstein medium.

By these methods tuberculosis was confirmed in 22 (31%) of the patients. Tuberculosis was demonstrated by other means in 3 further cases, bringing the total number of tuberculous effusions to 25 (35%). Bacteriological examination of the pleural exudate produced only three positive results. The authors point out that if those few cases in which the diagnosis could be made on other grounds were excluded, thoracoscopy was diagnostic in no less than 28% of the effusions. No condition other than tuberculosis was found during the investigation, although in 5 patients a haemothorax, possibly traumatic in origin, was suspected.

K. C. Robinson

1306. Differential Diagnostic Importance of Minor's Test in Tumours of the Thorax. (Дифференциально-диагностическое значение пробы Минора при опухолях грудной полости)

P. P. FIRSOVA. *Клиническая Медицина* [Klin. Med. (Mosk.)] 34, 71-76, No. 12, Dec., 1956. 3 figs.

Tumours arising from the sympathetic chain in the thorax, such as neuromata, neuromyxomata, and ganglioneuromata, are not uncommon. The presence of such a tumour can generally be demonstrated radiologically, but its exact nature cannot be determined from the x-ray appearances and the symptomatology is not usually characteristic. Indeed, it may be found on routine x-ray examination of an apparently healthy person. In other cases Horner's syndrome may be present, with pain in one or other side of the chest. In the diagnosis of such cases the author has found Minor's sweating test of great value. Out of 15 patients with a provisional diagnosis of neurinoma of the thorax,

5 gave a positive reaction to Minor's test; in all these cases histological examination of the tumour confirmed the diagnosis. In 6 cases the reaction was negative, and in these tumours of other types were found—including plasmacytoma, fibroma, mediastinal cyst, and even carcinoma of the lung.

The test was carried out as follows: the patient was given 1 g. of aspirin followed by one or two cups of hot tea, and 10 to 15 minutes later an ointment of iodine and castor oil was applied to the face, neck, thorax, upper part of the abdomen, arms, and back; as soon as the skin was dry it was powdered with fine starch, and the patient was then placed under a cradle and given a hot-air bath. Absence of sweating in any area was shown by failure to develop a dark violet colour. This phenomenon occurring in the area supplied by the sympathetic ganglia at the level of the tumour as seen in the radiograph is diagnostic of a neurinoma.

Details are given of 3 illustrative cases, 2 with a positive reaction and one (due to a fibroma) with a negative reaction, the tumours varying in size from 2×2 cm. to 12×10×8 cm. (the fibroma). L. Firman-Edwards

LUNGS AND BRONCHI

1307. An Evaluation of the Clinical Significance of Clubbing in Common Lung Disorders

L. CUDKOWICZ and D. G. WRAITH *British Journal of Tuberculosis and Diseases of the Chest* [Brit. J. Tuberc.] 51, 14-31, Jan., 1957. 6 figs., bibliography.

Although clubbing of the fingers has been recognized since Hippocrates described it, the cause is not well understood. It is generally accepted that there is an increased blood flow in the digits, mainly passing through arteriovenous anastomoses away from capillaries, thus inducing anoxic proliferation of fibrous tissue in the terminal segments of the digits. In an attempt to find the cause of this increased blood flow the authors studied the clinical features in 24 cases of drumstick clubbing due to a wide variety of pulmonary diseases seen at St. Thomas's Hospital, London. The symptomatology was very variable, no one feature indicative of a specific lung lesion emerging. Constant crepitations were heard in a part of the lung in 14 patients, but other signs were inconstant. There was a reduction in the two-second timed vital capacity in all, but maximum breathing capacity over 15 seconds showed much greater fluctuations and was within normal limits in 5. Similarly no constant abnormality was found in the chest radiograph, electrocardiogram, haemoglobin value, or arterial oxygen saturation in any of these cases. None of the patients had hypertension, and many had a high haemoglobin value with normal arterial oxygen saturation, findings which, it is suggested, might be significant.

In the authors' view the absence of a common clinical factor indicates that the cause of clubbing is in the abnormal lung tissue; they suggest that this may be the presence of pre-capillary bronchopulmonary anastomoses (described by Cudkiewicz and Armstrong, *Brit. J. Tuberc.*, 1953, 47, 227; *Abstracts of World Medicine*, 1954, 15, 406). They also consider that studies of pressure in the pulmonary arteries in such cases may be of value and they hope to publish a report on this subject later.

[This paper, which includes an excellent review of the literature on clubbing, should be read by all interested in this subject.]

A. Gordon Beckett

1308. Plane Atelectasis. (L'atélectasie-plane)

P. BROUSTET, H. BRICAUD, H. LEFORT, P. L. MARTIN, G. CABANIEU, P. MULLION, J. C. CHIGNON, and F. FONTAN. *Presse médicale [Presse méd.]* 64, 2109-2112, Dec. 19, 1956. 6 figs.

The authors describe and discuss a benign pulmonary condition to which they give the name "plane atelectasis", and report 9 cases observed at the Hôpital du Tondu, Bordeaux. The condition was first described by Laurell and Hülten in 1928. The clinical features are indefinite, but usually comprise cough, chest pain, dyspnoea, scattered rales, and sometimes tubular breathing. The diagnosis can be made only by radiography, when the characteristic feature of the condition appears as one or more narrow horizontal bands of shadowing in the lower or middle lobe of the lung. These shadows disappear temporarily after deep breathing or after injection of adrenaline. It is usual to find in association with this condition one of a variety of diseases of the pulmonary, cardiovascular, or gastro-intestinal systems. The bronchoscopic appearances are normal.

The authors consider that the lesions are due not to passive pulmonary collapse, but to true active atelectasis, and that they can be attributed to neurovegetative disturbances originating from disease in the thorax or abdomen and causing reflex contraction of pulmonary smooth muscle. The condition is benign, and the symptoms and signs disappear when the fundamental causal condition is treated.

Bernard Isaacs

1309. Six Cases of Traumatic Rupture of the Bronchus

M. BATES and H. J. BEARD. *Thorax [Thorax]* 11, 312-323, Dec., 1956. 21 figs., 8 refs.

Writing from the North Middlesex Hospital, London, and Kelling Hospital, Norfolk, the authors describe in detail 6 cases, all in children, of traumatic rupture of the bronchus.

On examination of 2 of the patients 21 and 10 years respectively after the rupture occurred bronchoscopy and bronchography showed that the damaged bronchus was completely occluded and the lung collapsed. Both these patients showed good chest development with no contraction of the hemithorax on the affected side, and they enjoyed good health apart from a tendency to bronchitis. The third patient was injured by a heavy tractor wheel in 1953 at the age of 7; 15 days after the accident he still had a pneumothorax with an airless lung, and

left pneumonectomy was carried out. At operation a tear was found in the back wall of the left main bronchus extending into the upper-lobe bronchus. This patient made a good recovery and remained well. In the 4th and 5th patients, who were both injured in motor accidents, the lung remained collapsed despite repeated bronchoscopy and attempts to dilate the bronchus. Thoracotomy was therefore undertaken, in each case 3 months after the rupture. In one case the two ends of the divided left main bronchus were both healed over with fibrous tissue, and were separated by a gap of 2 inches (5 cm.); in the other the right main bronchus was replaced over a distance of 1.5 cm. by a fibrous cord. In both patients the severed ends of the bronchus were successfully anastomosed and aeration of the lung carried out. Subsequent follow-up examinations, which included bronchoscopy, showed no significant abnormality. The 6th case was in a boy aged 2 who "choked on a bread crumb". A radiograph of the chest showed mediastinal emphysema, and a few days later obstructive emphysema of the left lung developed. A further radiograph 3 weeks after admission showed that the obstructive emphysema had given place to atelectasis of the left upper lobe. However, later films showed improvement, with a gradual return to normal in about 6 months. This sequence of events was regarded as being due to injury of the left bronchus. In this case the only treatment given was injections of penicillin, postural drainage, and physiotherapy.

The authors note that bronchial rupture is more common in children and that the site of the rupture is usually near the main carina. There may be no fracture of the ribs. A pneumothorax is usually present, and mediastinal emphysema is important evidence of rupture of the tracheal, bronchial, or more rarely the oesophageal wall. Haemoptysis is uncommon. Bronchoscopy should always be performed, but only if the means for performing thoracotomy are at hand, since an uncontrollable pneumothorax may demand immediate operation. Open operation is usually required for atelectasis and it should be undertaken early; it is still practicable, however, even if the atelectasis has been present for some months. It appears that complete interruption of the bronchial vessels is no bar to the healing of a bronchial anastomosis.

K. C. Robinson

1310. The Solitary Pulmonary Nodule. A Ten-year Study Based on 215 Cases

E. W. DAVIES, J. W. PEABODY, and S. KATZ. *Journal of Thoracic Surgery [J. thorac. Surg.]* 32, 728-770, Dec., 1956. 18 figs., bibliography.

The authors have analysed the pathology of 215 solitary pulmonary nodules which they have resected at the Garfield Memorial Hospital (Georgetown University School of Medicine), Washington, D.C., since 1947. They found that 37% of the lesions were malignant and that 41% were granulomata. The hamartoma was the commonest benign lesion, while more than one-half of the granulomata were due to histoplasmosis. The incidence of malignant nodules was greatest in the decade 50-59 years.

In discussing the diagnosis they give particular emphasis to the importance of calcification as a means of excluding malignancy; minimal calcification was no certain indication that a nodule was benign, but heavy or central calcification was hardly ever found in malignant lesions. Cavitation was by no means an indication of benignity. They found that the patients in their series with carcinoma did well, 75% being alive 5 years after resection. The length of history was of greater prognostic significance than cell type. Their findings re-emphasize the importance of early thoracotomy in the diagnosis and treatment of the solitary pulmonary nodule.

[This is an exhaustive and detailed study and the original paper is well worth reading in its entirety.]

J. R. Belcher

1311. Pulmonary Complications of Perforated Peptic Ulcer

B. T. LE ROUX. *British Journal of Surgery* [Brit. J. Surg.] 44, 342-347, Jan., 1957. 8 figs., 8 refs.

1312. Spontaneous Pneumothorax as a Complication of Pulmonary Sarcoidosis

N. WYNN-WILLIAMS and J. B. SHAW. *British Medical Journal* [Brit. med. J.] 1, 83-84, Jan. 12, 1957. 4 refs.

The authors report 4 cases of spontaneous pneumothorax occurring in patients with proved sarcoidosis. After careful scrutiny of the literature they found only 5 other reported cases—a surprisingly low frequency not easily explained. They suggest that although in some instances a pneumothorax due to this cause may be regarded as a complication of pulmonary tuberculosis, this cannot be the only explanation, and that more probably its occurrence in sarcoidosis is either frankly uncommon or taken for granted. They consider rupture of an emphysematous bulla, attributable to the sarcoid process in the lungs, to be the cause of pneumothorax in such cases.

In all their patients (aged 44, 54, 28, and 34 years respectively) sarcoidosis was histologically demonstrated—in the first, post mortem, the second by liver biopsy, the third by lung biopsy, and the fourth by lymph-node biopsy. All the patients had radiographic appearances in the lung fields suggestive of sarcoidosis and all gave a negative skin reaction to 1 in 100 or 1 in 10 old tuberculin. Two patients (aged 54 and 28 years) had bilateral pneumothorax. The treatment was that common to spontaneous pneumothorax from whatever cause.

[It does not seem certain that pneumothorax in the first two of these cases was directly due to sarcoidosis: in the first because the patient had been known to have had asthmatic episodes for at least 16 years before sarcoidosis was diagnosed, so that pulmonary emphysema may well have been present before the other disease occurred or became significant; and in the second because the patient's age made unrelated pulmonary emphysema quite possible. The possibility that emphysema and sarcoidosis may have existed coincidentally and without aetiological relationship in these cases is

not discussed. The question remains to what extent pulmonary sarcoidosis is capable of producing local emphysematous bullae which may cause pneumothorax.]

Raymond Parkes

1313. Consumption of Tobacco and Mortality from Malignant Tumours of the Respiratory Tract in Italy. (Consumo dei tabacchi e mortalità per tumori maligni dell'apparato respiratorio in Italia)

V. ROMEO and L. FERRI. *Annali dell'Istituto "Carlo Forlanini"* [Ann. Ist. "Carlo Forlanini"] 16, 233-243, 1956. 1 fig., 22 refs.

The authors, working at the Carlo Forlanini Institute, Rome, have correlated mortality from malignant disease of the respiratory tract (data supplied by the Central Institute of Statistics, Rome) with tobacco consumption (as detailed by the Italian State Tobacco Monopoly) in the various regions of Italy. The population at risk was estimated by taking the adults aged 21 years and over, including all men but subtracting four-fifths of the women, these being assumed to be non-smokers. The possibilities of error in this estimate are admitted, but are claimed to be inevitable in investigations of this type.

In general, in those regions where there was a much higher consumption of tobacco per head than the national average there was also a much higher incidence of respiratory malignant disease and vice versa, with the sole exception of Piedmont, where a very high incidence of respiratory cancer was associated with a low consumption of tobacco. No explanation has been found for this exception. This general relationship, however, was a crude one only, and differences in the incidence of respiratory cancer were not proportionate to differences in tobacco consumption.

Arnold Pines

1314. Lung Cancer and Other Causes of Death in Relation to Smoking. A Second Report on the Mortality of British Doctors

R. DOLL and A. BRADFORD HILL. *British Medical Journal* [Brit. med. J.] 2, 1071-1081, Nov. 10, 1956. 1 fig., 19 refs.

On October 31, 1951, the authors sent a questionnaire to 59,600 men and women on the Medical Register in the United Kingdom asking for information about their smoking habits. Of the replies, 40,701 (males 34,494, females 6,207) were sufficiently complete for analysis, tobacco consumption being assessed at that date or at the most recent date in the case of those who had given up smoking. These doctors have been followed up until March 31, 1956, and particulars of the cause of each death occurring amongst them obtained from the Registrars-General and other sources. During the 53 months 1,854 deaths were reported, but the authors have confined their analysis to the mortality experience of men aged 35 years and over, involving 1,714 of these deaths. (The data for women are at present insufficient for analysis (106 deaths, 2 from lung cancer).)

Lung cancer was the certified cause in 82 of these 1,714 cases, and was a contributing factor in a further 3. Confirmation of the diagnosis was obtained in all but one case. Age-standardized annual death rates per

1,000, computed separately for heavy smokers (daily average 25 g. of tobacco or more), medium smokers (15 to 24 g. daily), light smokers (1 to 14 g. daily), and non-smokers were respectively: from all causes 18.84, 14.94, 14.92, and 13.25; from lung cancer 1.66, 0.86, 0.47, and 0.07; from other cancer 2.63, 1.56, 2.01, and 2.04; from other respiratory diseases 1.41, 1.11, 1.00, and 0.81; and from coronary thrombosis 5.99, 4.60, 4.64, and 4.22. The χ^2 test shows the rates to be significantly higher among heavy smokers than among non-smokers for cancer of the lung and for all causes. A progressive increase in death rate from cancer of the lung with amount smoked is demonstrated for each of four separate age groups.

Further analysis of the data demonstrate that (a) the death rate from cancer of the lung among cigarette smokers was higher than that among pipe smokers (1.25 and 0.38 per 1,000 respectively), this difference still being significant if standardized for amount smoked; and that (b) among men who had smoked at any time, the death rate from cancer of the lung was highest in those still smoking and lowest in those who had given up for 10 years or more. There was an over-all increase in mortality from coronary thrombosis with the amount smoked which was, however, most pronounced in men under 55. Death rates from chronic bronchitis, pulmonary tuberculosis, and peptic ulcer showed a steady but less marked increase from non-smokers to smokers.

The authors discuss at some length the question of the bias which might have arisen in the diagnosis of cause of death or in the population at risk. They suggest that the evidence presented supports the hypothesis of a direct association of smoking with carcinoma of lung, in so far as the mortality from cancer of other sites showed no inverse relationship, and since the fact that smoking habits differ very little in urban and rural districts implies that the observed differences were not due to differential exposure to atmospheric pollution.

R. H. Cawley

1315. Occurrence and Aetiology of Lung Cancer in Norway in the Light of Pathological Anatomy

L. KREYBERG. *British Journal of Preventive and Social Medicine* [Brit. J. prev. soc. Med.] 10, 145-158, Oct., 1956. 7 figs., 17 refs.

In Norway the mortality from lung cancer is low compared with that in many other countries. There has been a progressive increase since the early 1930s, but this has been substantiated only among males living in towns. Histological examination shows that the male preponderance of certain histological types (Group I: squamous-, large-, and small-cell carcinomata) has increased throughout the period, but for other types (Group II: adenocarcinomata, bronchiolar-cell carcinomata, adenomata, and salivary-gland-type tumours) the sex ratio has not altered. Among males, but not females, there has been an increase in the proportion of Group-I tumours. Moreover, the age distribution of patients with tumours of these two types is entirely different, the incidence of Group-I tumours having a maximum in the 5th and 6th decades. Analysis of 300 personal cases shows that the Group-II tumours have

been drawn equally from all areas of the country, but that the Group-I tumours come predominantly from the towns. It is concluded that the increase in lung cancer in women reflects improvement in diagnostic methods, but that a new carcinogenic situation has arisen which has brought about an increase in Group-I cancers among men resident in the towns. It is unlikely that the increase is due to general atmospheric pollution, since the ratio of Group-I to Group-II tumours is higher in small non-industrial towns than in industrial centres (excluding the 3 largest towns) and because even in Oslo pollution is only of the same order as that found in a Welsh coastal village. Personal material reveals no special occupational risk of lung cancer. Group-II cancers in both men and women are equally common in the 3 principal occupational categories: (1) open air and house work; (2) clerical, commercial, and professional; and (3) "dusty" work. Group-I cancers were substantially commoner in Category 3 than in Category 1, but they were nearly as common in Category 2 as in Category 3.

Analysis of the smoking habits of the patients and of samples of the general population showed: (1) No difference between the smoking habits of male or female patients with Group-II tumours and those of the general population of the same sex and age group. (2) A steady increase in the Group-I:Group-II ratio in males with increase in the amount of tobacco smoked; smoking appears to be responsible for 4 out of 5 Group-I tumours in Norwegian men. (The number of Group-I tumours occurring in women was too small for similar analysis.) (3) A smaller consumption of tobacco by men in "dusty" occupations than men engaged in clerical and professional work; industrial dust may perhaps aggravate the injury caused by tobacco smoking. (4) The relationship between lung cancer and pipe smoking (if any) is less marked than that with cigarette smoking. (5) Men in smaller towns with "fresh" air are more often cigarette smokers than men in smaller industrial centres with "polluted" air; this may account for the finding of a higher proportion of Group-I tumours in men in the "fresh air" towns. (6) The Group-I:Group-II ratio in non-smokers is higher for men than for women; this cannot be ascribed to occupational factors, and an intrinsic sex difference in the response of the lungs to external agents is possible.

Richard Doll

1316. Lung Cancer in Women. A Study of Environmental Factors

E. L. WYNDER, J. BROSS, J. CORNFELD, and W. E. O'DONNELL. *New England Journal of Medicine* [New Engl. J. Med.] 255, 1111-1121, Dec. 13, 1956. 6 figs., 17 refs.

Female mortality from lung cancer has increased less rapidly than male—early in the century the male:female ratio was about 1½:1; now it is 5:1 or more. The distribution of the histological types is also different in the two sexes; in men the proportion of adenocarcinoma is variously reported as between 5 and 20%; in women it is nearer 50%.

In the present study data were collected about 196 women who were treated for lung cancer at 11 hospitals

in New York or Boston during the years 1953-5; additional data were obtained by interview with the patient or by questionnaire sent to the close relatives in 105 cases. Comparison between the results obtained by various methods of treatment showed no important differences and results for the whole series were therefore pooled. Of the 196 tumours, 42% were adenocarcinoma, 32% were epidermoid carcinoma, 18% were anaplastic carcinoma, and 8% were unclassified. Patients with epidermoid cancer were, on average, somewhat younger than those with adenocarcinoma. No differences were found in the distribution among the main occupational groups between women with lung cancer of the various histological types and a control group of 1,304 women with benign or malignant growths at other sites. Neither were there any important differences in the educational level or place of residence of the various groups of patients. Women with epidermoid cancer reported chronic cough more often than women with adenocarcinoma and more often than the control patients. Women with epidermoid or anaplastic cancer were more often smokers and much more often heavy smokers than the control patients; on the other hand the smoking habits of the patients with adenocarcinoma did not differ significantly from those of the controls.

In a separate study a comparison was made between the smoking habits of 205 white males and 205 white females who were matched for age, educational level, and diagnosis (benign condition or non-respiratory cancer). Among the men the proportion of non-smokers varied between 10 and 20% irrespective of age; among the women the proportion increased from just over 50% at ages 30 to 39 to nearly 90% at ages 60 to 69. At all ages the proportion of heavy smokers was greater among men, and among women the proportion fell almost to zero at the older ages. The results obtained for women without lung cancer were practically identical with those obtained for a nation-wide sample conducted by the Bureau of the Census.

It is concluded that cigarette smoking substantially increases the risk of developing epidermoid cancer of the lung, but not, probably, of adenocarcinoma, and that differences in smoking habits can probably account for the extent of the preponderance of cases among men.

Richard Doll

1317. Review of 910 Cases of Bronchial Carcinoma with Results of Treatment

W. F. NICHOLSON, M. FOX, and A. G. BRYCE. *Lancet* [Lancet] 1, 296-298, Feb. 9, 1957. 3 figs., 10 refs.

The authors review 910 cases of bronchial carcinoma treated at the Royal Infirmary, Manchester, between 1948 and 1954. There were 840 male patients and 70 female, a proportion of males to females of 12 to 1, and the average ages were 55 and 53 years respectively.

The main symptoms on diagnosis were a change in character of the cough, breathlessness, haemoptysis, fever due to recurrent bronchial obstruction with infection, and chest pain. Hoarseness, dysphagia, pain down the arm, venous obstruction, and severe weight loss

were late symptoms; cases manifesting pulmonary osteoarthropathy were all found to be inoperable. During the 7-year period under review the interval between onset of symptoms and diagnosis remained constant at just over 6 months. In 15 cases the neoplasm was asymptomatic and was diagnosed only at mass radiography; 3 of these patients survived more than 3 years after surgical removal of the tumour.

In regard to the site of origin of the neoplasm the two lungs were affected about equally, but the upper lobes (left 24.5%, right 22.5%) were involved more often than the lower lobes (left 15%, right 19%). In the remaining cases the site was in the main bronchus, middle lobe, or lingula; the last-named was the site in only 8 cases (0.9%), and it proved a favourable site in terms of surgical survival (37%). Adequate histological details were available in 414 cases, and showed that 56% of the tumours were squamous-cell carcinoma, 21% oat-cell carcinoma, 16% spheroidal-cell carcinoma, and 6% were adenocarcinoma; a further 1% represented mixed salivary tumours and sarcomata. Thoracotomy was performed on 340 (37%) of the patients, 191 (56%) of these undergoing radical resection (52% of all thoracotomies in the period 1948-52, increasing to 69% in the period 1952-4). Studies of survival showed that the prognosis in oat-cell and spheroidal-cell carcinoma was hopeless. The fact that these cell types were relatively more common in the authors' female patients may account for the poor results of surgery; thus out of 53 women seen up to 1952, only 2 lived for 3 years or more after resection. Of the 132 patients treated radically between 1948 and 1952, 44 (33.3%) survived for 3 years, representing 6% of the 720 cases seen in that period, while 25 of these patients are still alive after 5 years or more, that is, 28% of the 132 patients undergoing radical resection, or 5.5% of all cases.

C. A. Jackson

1318. Brain Metastases from Primary Bronchial Carcinoma: a Statistical Study of 741 Necropsies

S. GALLUZZI and P. M. PAYNE. *British Journal of Cancer* [Brit. J. Cancer] 10, 408-414, Sept., 1956. 1 fig., 32 refs.

The incidence of brain metastases from bronchial carcinoma was studied in the necropsy reports relating to 647 patients dying from the disease in 8 London hospitals between 1948 and 1952. Metastases were found in the brain in 25.7% of these cases, this organ being surpassed only by the liver and adrenal glands in frequency of involvement. Metastases were common from undifferentiated carcinoma and adenocarcinoma, but relatively uncommon from squamous-celled carcinoma. As regards distribution of single metastases only, the authors found no significant deviation from the proportions which would be expected to lodge in the cerebrum (62%) and the cerebellum (38%). They do not consider that the results of this investigation "add weight to the suggestion" that the increase in the certification of deaths due to bronchial carcinoma reflects a real increase in the incidence of the disease.

R. G. Rushworth

Otorhinolaryngology

1319. Anesthesia for Surgery of the Nose, Pharynx, Larynx, and Trachea

D. C. MOORE and J. F. TOLAN. *A.M.A. Archives of Otolaryngology* [A.M.A. Arch. Otolaryng.] 64, 275-288, Oct., 1956. 14 figs., 34 refs.

The authors consider that barbiturates offer little protection against toxic reactions from a local analgesic, and may mask early danger signs. They prefer to use intravenous chlorpromazine for sedation. They find tachycardia "not unusual" but have noted no other untoward effects. On the other hand they have occasionally experienced restlessness or respiratory difficulty which has had to be corrected with intravenous pentobarbitone. Sometimes there is a severe fall in blood pressure which cannot be corrected with adrenaline because chlorpromazine counteracts it. They advocate succinylcholine as an aid in intratracheal intubation; before using it they observed 8 cases of granuloma of the vocal cords following intubation in a period of 5 years; in one a vocal cord was "completely sheared off".

[The reader is left with the impression that the dangers of local analgesia are considerable, and that some of the prophylactic measures advised are themselves not too safe.]

F. W. Watkyn-Thomas

1320. Experiments upon the Total Inhibition of Stammering by External Control, and Some Clinical Results

C. CHERRY, B. M. SAYERS, and P. M. MARLAND. *Journal of Psychosomatic Research* [J. psychosom Res.] 1, 233-246, Nov., 1956. 2 figs., 8 refs.

Production of speech involves a closed-cycle feed-back action, the speaker, by his perceptions, continually monitoring and checking his voice production. In this paper from the Imperial College and St. Mary's Hospital, London, the authors assume that stammering represents functionally a type of relaxation oscillation caused by instability in the feed-back loop, the determining defect being perceptual rather than motor. A demonstration of this is the marked speech disturbance which occurs in a person of normal speech habits when a tape recording of his speech is played back to him while he is speaking but delayed by about $\frac{1}{10}$ to $\frac{1}{2}$ second—so-called delayed play-back speech. Stammerers speak with little or no difficulty if "shadowing" the speech of a normal person and also in simultaneous reading; in the latter case the improvement is maintained even if the control reader suddenly switches to another text or to gibberish. Control of the acoustic environment of speech or speech-like sounds is thus shown to provide some control of the stammerer's speech difficulty. The authors consider which components of the stammerer's own speech (perceived in self-monitoring) take control and appear to mediate stammering. Tests described might appear to indicate that bone-conducted sounds are of special significance and that low and very low frequencies are alone of importance.

T. A. Clarke

1321. Mobilization of the Stapes without Incision. A Preliminary Report on Mobilization of the Stapes by Vibrations Originating at the Short Process of the Malleus

M. C. MYERSON. *A.M.A. Archives of Otolaryngology* [A.M.A. Arch. Otolaryng.] 64, 373-376, Nov., 1956. 4 figs., 5 refs.

The author recently described (*A.M.A. Arch. Otolaryng.*, 1956, 64, 85; *Abstracts of World Medicine*, 1957, 21, 191) a method of mobilizing the stapes by applying a vibrating rod to the incudo-stapedial articulation. As a further development of this method he now, under local analgesia and using a speculum (without any incision of the membrane), applies the forked rod to the short process of the malleus and causes it to vibrate, as he did for the incudo-stapedial joint. He has applied the method to 3 cases of otosclerotic deafness with good results, the only ill effect being a transient swelling of the membrane due to extravasation of blood in one case, in a patient aged 78. All 3 patients experienced "momentary" vertigo.

F. W. Watkyn-Thomas

1322. The Cochleopalpebral Reflex in Normal Hearing and Hard of Hearing Persons

J. P. ALBRITE, R. A. BUTLER, and F. T. GALLOWAY. *A.M.A. Archives of Otolaryngology* [A.M.A. Arch. Otolaryng.] 64, 402-408, Nov., 1956. 2 figs., 2 refs.

Galambos *et al.* (*J. Speech Hear. Dis.*, 1953, 18, 373), using clicks as the stimulus, found that some patients with severe hearing loss exhibited the cochleopalpebral or "eye-blink" reflex at intensities only 20 to 30 db. higher than the stimulus needed to produce it in persons with normal hearing. They therefore suggested that the reflex might be used for the differential diagnosis between conduction deafness, in which a greater stimulus would be necessary, and nerve deafness with recruitment.

In the present study, carried out at the Walter Reed Army Medical Center, Washington, D.C., 40 subjects were investigated, 21 with normal hearing and 19 with "perceptive deafness" attributed to various causes; the stimulus used consisted of pure tones ranging from 500 to 4,000 c.p.s. in intensity. The results suggest that patients with "perceptive deafness" showed evidence of recruitment of loudness to this test, and further that those whose deafness was due to acoustic trauma responded to lower intensities than those whose deafness was due to other causes. Patients with conductive deafness required much stronger stimuli to produce the response.

The authors state that although these results are interesting, it cannot yet be taken as proven that they are directly due to the recruiting factor. It is possible, for example, that high-intensity stimuli could set up muscular contraction in the middle ear which would initiate afferent impulses which in turn could evoke the eye-blink response; while conversely, the stiffened ossicular chain present in conductive deafness could restrict the magnitude of such contractions.

F. W. Watkyn-Thomas

Urogenital System

1323. Effect of Hypotensive Drugs on Renal Function in Chronic Renal Disease

D. G. ABRAHAMS and C. WILSON. *Lancet* [Lancet] 1, 68-74, Jan. 12, 1957. 2 figs., 10 refs.

Observations are reported from the London Hospital on 32 patients—16 with chronic Type-I nephritis, 7 with Type-II nephritis, 4 with other forms of renal disease, and 5 with malignant essential hypertension—who were treated with ganglion-blocking agents with or without the addition of reserpine. In short-term observations there was no evidence that kidney function deteriorated in any way, as judged by concentration of urea and creatinine clearance, when the blood pressure was lowered by these drugs. Over a longer period of hypotensive treatment, although some patients showed progressive uraemia, there was no evidence that the advance of the disease was in any way related to blood-pressure reduction: in many cases there was no evidence of deterioration of kidney function. It appeared that hypotensive treatment was likely to be of long-term benefit where the creatinine clearance was over 50 ml. per minute initially and the blood urea level 60 mg. per 100 ml. or less. If the initial blood urea level was above 70 mg. per 100 ml. renal failure was likely to be progressive. *J. McMichael*

1324. The Radioisotope Renogram. An External Test for Individual Kidney Function and Upper Urinary Tract Patency

G. V. TAPLIN, O. M. MEREDITH, H. KADE, and C. C. WINTER. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 48, 886-901, Dec., 1956. 5 figs., 7 refs.

In studies carried out at the University of California School of Medicine, Los Angeles, the authors have applied external gamma-ray scintillation counting and recording techniques to the study of renal function. After extensive experiments on rabbits they have evolved the following clinical technique for obtaining a "diodrast renogram". A trace dose of "diodrast" (diodone) solution containing radioactive iodine (^{131}I) is injected intravenously, and three scintillation detectors over the chest and renal areas record the radioactivity in the blood and in the individual kidneys during the next 15 to 30 minutes. The form of the resultant graphs from the renal areas yields qualitatively reproducible data on the vasculature, tubular cell function, and patency of the upper urinary passages of each individual kidney, and (in experimental animals) the blood clearance rates of gamma radioactivity provide a rapid estimation of bilateral renal function.

In clinical studies curves which were diagnostic were obtained in cases of hydronephrosis and of acute ureteral obstruction due to calculus, and also in patients with only one functioning kidney. Cases of chronic glomerulonephritis, the nephrotic syndrome, and nephro-

sclerosis showed abnormal patterns, but these were not individually diagnostic. Abnormalities in cases of acute pyelonephritis were found to regress as renal tubular function and excretory capacity improved following antibiotic therapy. In all, 125 renograms have been performed and the results have been checked by the usual standard renal function tests. The diodrast renogram test is considered to be a safe, rapid, non-traumatic test which could replace intravenous pyelography, retrograde pyelography, and various renal function tests in many patients for purposes of diagnosis or estimation of progress. The technique is being further developed, in particular to yield more quantitative data.

T. B. Begg

1325. Clinical Experience with the Skeggs-Leonards Type of Artificial Kidney. Report on 46 Consecutive Patients

P. ANTHONISEN, C. BRUN, C. CRONE, N. A. LASSEN, O. MUNCK, and A. C. THOMSEN. *Lancet* [Lancet] 2, 1277-1281, Dec. 22, 1956. 4 figs., 11 refs.

In this paper from the Kommunehospital, Copenhagen, the authors report their experience with the Skeggs-Leonards artificial kidney in the treatment of acute renal failure. In this type of haemodialysing apparatus blood from the inferior vena cava is pumped at the rate of 400 to 700 ml. per minute through narrow spaces between layers of "cuprophane" sheets, each $11\ \mu$ thick and mounted between grooved rubber, presenting a dialysing surface of about 2 sq. metres, while saline at a rate of 3 litres per minute is pumped along the outer surface of the dialysing membrane in the opposite direction. The apparatus was used 78 times in the treatment of 46 patients.

Of 35 patients with severe uraemic signs complicating serious primary non-renal diseases, 11 survived after one to 4 treatments with dialysis, and one, treated with dialysis on 8 occasions for renal failure following barbiturate poisoning complicating the effect of an unknown haemolytic agent, eventually died from cachexia although renal function had become nearly normal. A further 4 patients with exacerbations of chronic pyelonephritis could not be saved, though the immediate effects of dialysis on the signs of uraemia were good. In one patient with acute glomerulonephritis life was prolonged by dialysis for many weeks. In 6 cases of bromide or barbiturate poisoning an excellent response was obtained; the elimination of the drug was remarkably accelerated, the serum bromide level in one case falling from 41 to 4 mEq. per litre after a few hours of dialysis. Lastly, in one case of severe hyperkalaemia after an overdosage of potassium a markedly abnormal electrocardiogram became normal during the dialysis, and the patient made a dramatic recovery. Dialysis should be used as early as possible in all suitable cases. *L. H. Worth*

Endocrinology

1326. Transplantation of Foetal Endocrine Glands. (Брефопластика желез внутренней секреции)

N. M. KADŪSEVA. *Проблемы Эндокринологии и Гормонотерапии* [Probl. Endokr. Gormonoter.] 2, 90-98, No. 6, Nov.-Dec., 1956. 4 figs., 20 refs.

From a survey of the literature the author concludes that there is good evidence to suggest that transplants of foetal endocrine glands are more likely to survive and function normally than transplants of adult endocrine tissues. At the Jaroslav Medical Institute foetal endocrine tissues are obtained from foetuses expelled at abortion induced medically in the 4th or 5th month of gestation. Tissue obtained from one foetus may be transplanted to a number of patients. In the selection of donors and recipients attention is paid to such factors as blood groups, biochemical relationships, and immunological properties. The transplants are usually inserted subcutaneously at McBurney's point in the right iliac fossa.

Out of her 20 years' experience of the method the author describes 2 cases of pituitary transplantation for hypopituitary dwarfism. The first case was that of a boy aged 15 who at the time of transplantation was only 110 cm. (43 inches) tall. Within 2 years after the operation he had gained 13 cm. (5½ inches) in height; the rate of growth was much quicker during the first year than during the second and a further transplant will be required. The second patient received his first pituitary transplant at the age of 16, with little beneficial result. At the age of 28 he was treated with thyroxine and repeated small blood transfusions (including blood from pregnant women) and 2 years of this therapy resulted in a height gain of 7 cm. (3 in.). At the age of 30 another transplantation was performed and during the succeeding 2 years the patient gained 15 cm. (6 in.) in height. A third transplant at the age of 32 resulted in a height gain of another 5 cm. in 2 years. In parallel with the improvement in stature the patient's sexual development also improved and at the age of 34 he first contemplated marriage.

The author suggests that this type of operation, though up till now not widely recognized, is capable of wide clinical application, but should be preceded by correction of any hypothyroidism that may be present.

Marcel Malden

1327. Total Free Tocopherols in the Serum of Patients with Thyroid Disease

S. POSTEL. *Journal of Clinical Investigation* [J. clin. Invest.] 35, 1345-1356, Dec., 1956. 8 figs., bibliography.

It has been suggested that there may be deficiency of tocopherols in patients with thyrotoxicosis. At Massachusetts General Hospital, Boston, the author has therefore determined the total free tocopherol concentration in the serum of 115 persons, this number including 34

patients with Graves's disease (of whom 5 had been receiving antithyroid treatment for 2 weeks before the tests), 18 who were clinically hypothyroid, 30 normal subjects, and 33 patients who were euthyroid but were suffering from a variety of other disorders.

A highly significant inverse relationship between the serum tocopherol values and the state of thyroid function was found. Hyperthyroid patients showed a mean tocopherol concentration of 0.74 mg., normal and euthyroid individuals a mean value of 1.2 mg., and hypothyroid patients 2.29 mg. per 100 ml. Changes in the serum tocopherol level were paralleled by changes in the serum cholesterol level in most, but not all, cases; tocopherol values returned to normal levels after treatment of the thyroid condition. There was no correlation between the degree of muscular disease and serum tocopherol levels, but it is considered possible that human thyrotoxic myopathy may be analogous to the muscular dystrophy due to vitamin-E deficiency in animals.

F. W. Chattaway

1328. The Causes of Congenital Myxoedema and the Genetic Aspects of Thyroid Diseases. (Les causes du myxoedème congénital et l'aspect génétique des maladies thyroïdiennes)

M. BERNHEIM, M. BERGER, R. UZAN, and J. CHAMBRON. *Semaine des hôpitaux de Paris* [Sem. Hôp. Paris] 32, 4104-4113, Dec. 26, 1956. 3 figs., 10 refs.

Congenital myxoedema is due to partial or total atrophy of the thyroid gland in the newborn infant. The authors have investigated 50 affected children and their families in order to ascertain how far the condition is due to genetic factors and how far to extrinsic factors acting on the foetus. Of the 50 children affected, 2 were sisters, otherwise there was only one case per family. Ten of the 49 mothers had some clinical thyroid anomaly, but the clinically normal mothers and fathers of the children showed abnormalities of thyroid function when their ability to fix radioactive iodine was tested. It was found that among the brothers of the myxoedematous children there was an increased mortality in the first months of life; and that both the brothers and sisters had anomalies of thyroid function like those of the parents.

The authors conclude that there is a genetic factor in congenital myxoedema and suggest that all thyroid disorders are genetically influenced. They consider that congenital myxoedema represents the homozygous form of the disease, whereas the heterozygotes may develop hypothyroid goitre or exophthalmic goitre according to individual differences of metabolism. Furthermore, they state that, in addition to the genetic factor, reduced placental permeability also plays a part in depriving the foetus of the maternal thyroid hormone.

M. C. G. Israël

ADRENAL GLANDS

1329. Renal Function in Primary Aldosteronism

H. P. DUSTAN, A. C. CORCORAN, and I. H. PAGE.
Journal of Clinical Investigation [J. clin. Invest.] 35, 1357-1363, Dec., 1956. 1 fig., 22 refs.

Renal function was studied in 3 proved cases of primary aldosteronism in each of which an adrenal cortical adenoma was removed. Before operation plasma clearance of PAH was depressed, but mannitol clearance was within the normal range; for several months after operation the plasma clearance of PAH remained depressed. In all cases maximum specific gravity of urine was low before operation and was slow to recover afterwards. The serum potassium level was also low, but the serum sodium level was within the normal range. In spite of hypokalaemic alkalosis the pH of the urine was persistently alkaline; after operation alkalosis was replaced by acidosis. Proteinuria was slight in all cases and diminished after operation. In 2 cases there was no remission in hypertension after operation; some degree of nephrosclerosis was believed to have been present. The pre-operative defect in water reabsorption during osmotic diuresis was considered to be a reversible one imposed by potassium deficiency. Normally, the kidney excretes an acid urine in potassium depletion despite alkalosis; in aldosteronism the urine is alkaline, and a tentative explanation of the mechanism of this is offered.

C. L. Cope

1330. Inhibition of Aldosterone Secretion by Amphenone in Man

A. E. RENOLD, J. CRABBÉ, L. HERNANDO-AVENDANO, D. H. NELSON, E. J. ROSS, K. EMERSON, and G. W. THORN. *New England Journal of Medicine* [New Engl. J. Med.] 256, 16-21, Jan. 3, 1957. 3 figs., 16 refs.

In a study at the Peter Bent Brigham Hospital, Boston, of the effect of "amphenone" on the production or release of aldosterone the amphenone was administered by mouth at intervals of 2 to 4 hours throughout the 24 hours, special precautions being taken to remove by means of ion-exchange resins coloured amphenone derivatives from the urine where these interfered with chemical estimations.

The compound was first administered for 3 days in doses of 6, 6, and 3 g. per day respectively to a patient suspected of having bilateral adrenocortical hyperplasia who was maintained on a limited sodium intake of 9 mEq. per day. There was a distinct sodium diuresis during the 3 days of treatment, followed by a marked rebound retention of sodium on cessation. Aldosterone disappeared from the urine under amphenone treatment, but showed a rebound increase in level on the 2nd and 3rd days after discontinuance of the drug. In another patient, a 39-year-old nurse with a history of unexplained anasarca, the urinary aldosterone secretion was 66 to 123 μ g. per day, the urinary 17-hydroxycorticoid and 17-ketosteroid excretion being within normal limits. The administration of amphenone on three separate occasions resulted in the reduction of the urinary aldo-

sterone excretion almost to normal values and the production of a significant sodium diuresis. Removal of an adrenal adenoma was followed by regression of the urinary aldosterone levels to normal limits. In a third patient with normal adrenal function who was being maintained on a sodium dietary intake of 9 mEq. daily the administration of 5.5 g. of amphenone daily for 3 days resulted in a markedly increased sodium output, from 1.5 mEq. on the day before treatment to 15 mEq. on the first day and 40 mEq. on the second and third days of treatment. On the fourth day, when treatment had been discontinued, the sodium excretion was still 49 mEq. per day, but returned to control levels on the succeeding days.

A significant sodium diuresis occurred after 17 out of 25 courses of amphenone therapy, with clear-cut sodium retention in 13 out of the 17 cases; unexplained failure to induce sodium diuresis was limited to 3 patients. Aldosterone excretion was significantly reduced in 11 out of 15 courses of therapy. In only one out of 8 patients whose control excretion of aldosterone exceeded 10 μ g. per day did the compound fail to reduce aldosterone excretion. The possible use of short-term courses of amphenone as a diagnostic procedure in hyperaldosteronism and sodium retention is discussed.

Norval Taylor

DIABETES MELLITUS

1331. Natural Course and Prognosis of Juvenile Diabetes P. WHITE. *Diabetes* [Diabetes] 5, 445-450, Nov.-Dec., 1956. 4 figs., 15 refs.

The author reviews 1,072 cases of juvenile diabetes seen at the Joslin Clinic (Tufts Medical School), Boston, in which the patients had survived 20 years or more. Of these, 82% are still alive, 16% have died, and 2% could not be traced. Many of these patients have achieved a high socio-economic status; thus 20% of them are in professions, compared with 6% of the general population.

The age at onset (with a peak at 11 years) and the equal sex distribution in this series was typical of juvenile diabetes. In 57% of cases there was a family history of diabetes, but only 13% of the patients had a diabetic parent and only 1% had offspring with diabetes, suggesting that the disease is inherited as a Mendelian recessive gene. The onset was acute, typically in one day, or week, or month, in some cases accompanied by coma. Subsequently remissions occurred in one-third of the patients, the glucose tolerance test result in many cases returning to normal. Later there was intensification of the diabetic state, the insulin requirement being usually affected more by linear growth than by increase in weight. A total or near total diabetic state was eventually reached by all. In 29 of the 31 cases studied at necropsy there was diminution in the size and number of the islets and cellular differentiation.

The majority of these patients achieved normal height, but the weight after the age of 20 was just normal or more often slightly subnormal. In 28% of the females there was a late onset of periods, but in later life "hypo-

ovarianism" was not present and sterility was not a problem. However, in 473 pregnancies the foetal wastage was high, being 40% compared with 13% in normal women; the abortion rate was 2½ times and the perinatal death rate 6 times the normal. The rate of foetal loss in the wives of diabetic men was normal. All these patients suffered, in varying degrees of intensity, the major complications of diabetes, namely, coma, infections, neuritis, and vascular damage. Thus 52% of the females had severe ketosis or coma, 15% having recurrent attacks, while 39% of males had ketosis, with recurrences in 12%. Abscesses and carbuncles were common, occurring in about one-third of the cases. Pyelonephritis occurred in 12% of females but in only 2% of males, and tuberculosis in 4%. Neuropathy occurred in 26% of females and 20% of males, the commonest form being acroneuritis, with gastro-intestinal neuropathies in second place. Vascular damage was however the most serious complication and was the cause of death in 148 (87.5%) of the 169 fatal cases. The cardio-renal-vascular lesions were not seen within the first 5 years of the diabetes and rarely in the first 10 years, but by 15 years 19% of the patients had a retinopathy and 14% calcified arteries. At 35 years after the onset 94% of patients had calcified arteries, 93% retinopathy, 53% hypertension, and 44% nephropathy. Although the incidence of disabilities arising from vascular damage was appreciable, there is increasing evidence that in a certain number of these patients the vascular lesions reach a static phase, this favourable outcome being best seen in the retina.

There was a statistically significant correlation between poor biochemical control of the diabetes and the frequency and severity of the vascular lesions in these juvenile diabetics, but no such relationship between a low-protein diet and the vascular lesions. The author believes that the tendency to develop vascular change and hyperglycaemia is inherited as a recessive defect and that poor control of the diabetes markedly affects the vascular response.

A. Gordon Beckett

1332. Spontaneous Hypoglycemia as an Early Manifestation of Diabetes Mellitus

H. S. SELTZER, S. S. FAJANS, and J. W. CONN. *Diabetes* [Diabetes] 5, 437-440, Nov.-Dec., 1956. 1 fig., 10 refs.

During the 6-year period 1950-6 the authors have observed at the University of Michigan Hospital, Ann Arbor, 110 patients in whom the result of an oral glucose tolerance test was diagnostic of mild diabetes mellitus but which also showed a steep secondary hypoglycaemic phase. The lowest blood sugar values observed during the test were between 25 and 50 mg. per 100 ml. (mean 42 mg.) and these always appeared between the 3rd and 5th hours.

Of these 110 patients, 70 were men and 40 women, their ages ranging from 19 to 80 years. Obesity was present in 37, and there was a family history of diabetes in 48. About two-thirds (76) of these patients came to hospital because of troubles referable to hypoglycaemia, postprandial symptoms being the chief complaint in 67. In the remainder, who had no symptoms of hypo-

glycaemia, the glucose tolerance test was carried out, since diabetes was suspected. The diabetes was mild in all cases. Secondary hypoglycaemia did not occur when the fasting blood sugar was above 130 mg. per 100 ml.

The authors suggest that an early defect in diabetes mellitus is a diminution of the speed of mobilization of insulin in response to a rising blood sugar concentration, that in this early phase the capacity to produce insulin is about normal, and that this initial hyperglycaemia finally provides a supernormal stimulus resulting in an outpouring of enough insulin to produce hypoglycaemia. Routine diabetic management, usually with diet alone, effectively controls the hypoglycaemic symptoms.

A. Gordon Beckett

1333. A Trial of Oral Treatment of Diabetes with D 860. (Essais de traitement oral du diabète par le D 860)

R. MOREAU, R. DEUIL, A. SARRAZIN, and P. M. DE TRAVERSE. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [Bull. Soc. méd. Hôp. Paris] 72, 788-799, Oct. 26, 1956. 4 figs.

Experience of the use of a sulphonamide, "D 860", in the treatment of diabetes since January, 1956, is reported. The action of the drug on 27 normal subjects was first studied: a single dose of 2 g. was found to produce a fall of 20 to 30% in the fasting blood sugar level for 4 hours after administration and to have some persisting hypoglycaemic action after 24 hours, even though the subject had taken two normal meals in the meantime.

A group of 100 patients were then selected for treatment, all having diabetes of late onset which was poorly controlled by diet alone or with moderate amounts of insulin. Patients showing loss of weight were excluded. Control was achieved with D 860 given by mouth in 41 of the 46 cases previously treated with insulin and 53 of the 54 cases previously treated with diet alone. Details are given of the results obtained in a number of illustrative cases. No toxic effects have so far been observed by the authors. The dosage recommended is 3 g. daily in divided doses for about one week followed by a maintenance dose of 2 g. daily in successful cases which in some instances can be reduced to 1 g. daily. Increasing the dose in unsuccessful cases is useless.

It is claimed that by comparing the glucose tolerance curves obtained before and half an hour after the administration of a single dose of 3 g. of D 860 it is possible to assess the response of the patient to the drug.

T. D. Kellock

1334. Mechanism of Action of BZ 55 in Human Diabetes. (Mécanisme d'action du BZ 55 dans le diabète humain)

P. A. BASTENIE, J. R. M. FRANCKSON, R. DE MEUTTER, and V. CONARD. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [Bull. Soc. méd. Hôp. Paris] 72, 799-802, Oct. 26, 1956. 29 refs.

The authors, working at the Hôpital Saint-Pierre, Brussels, have investigated the mode of action of "BZ 55" (carbutamide) on the glucose tolerance of human diabetics.

Observations were made on 18 patients with diabetes, only one of whom had ever been ketotic. Tests were carried out on each patient before starting a course of carbutamide and repeated 6 to 10 days later and again after several months. In each case the rate of fall of the blood sugar level was noted (1) after an intravenous dose of glucose (0.66 ml. of a 50% solution per kg. body weight), (2) after a similar dose to which had been added 0.1 unit of insulin per kg., and (3) after the same dose of insulin unaccompanied by glucose. The curves recording the fall of the blood sugar level were analysed mathematically.

The rate of fall after the intravenous injection of glucose was found to be unchanged by the administration of carbutamide, and it is concluded that the rate of assimilation of glucose is unaffected by the drug. Similarly the rate of fall after a mixed injection of glucose and insulin was unaffected by the drug, showing that the activity of insulin was unchanged. The curve following the intravenous injection of insulin alone on the other hand was modified by the administration of carbutamide. One of the authors has previously demonstrated that two factors can be calculated from this curve in healthy subjects, one representing the direct hypoglycaemic effect of the insulin and the other the output of glucose by the liver. Analysis of the curves obtained in the present investigation showed that after the administration of carbutamide the effect of insulin was unchanged, this finding confirming the conclusions drawn from the mixed glucose and insulin test, whereas the glucose output of the liver showed a marked fall.

One of the features of diabetes is the uncontrolled gluconeogenesis that takes place in the liver, and the authors' main conclusion is that carbutamide exerts its beneficial effect by reducing this abnormal activity, probably by interfering with the action of glucose-6-phosphatase.

[An English translation of this paper has since been published in the *Lancet* (1957, 1, 504).]

T. D. Kellock

1335. Thrombocytopenia and Leucopenia following Carbutamide

J. C. PHEMISTER. *British Medical Journal* [Brit. med. J.] 1, 199-204, Jan. 26, 1957. 1 fig., 19 refs.

The author, in this paper from the University of Edinburgh, describes the haematological findings in 40 diabetics given carbutamide in a dosage of 1.5 g. daily for 7 days and thereafter in a maintenance dose of 0.5 to 1.5 g. daily. The majority of the patients were middle-aged or elderly women with mild diabetes of some years' duration; a group of 50 diabetics not given carbutamide served as controls. Leucopenia was common at the start of treatment, but was transitory; in one patient a severe leucopenia developed which continued after cessation of treatment.

Depression of the platelet count was observed in many patients, but spontaneous purpura was seen only in 2. In one of these 2 cases purpura was associated with thrombocytopenia and a strongly positive reaction to Hess's test; in this case tolbutamide also caused depres-

sion of the platelet count. The purpura in the second case was probably allergic in type and was unassociated with any fall in the platelet count. The author concludes that carbutamide is not a safe drug for routine use in diabetes, and suggests that its effect on capillary fragility requires further investigation.

I. McLean Baird

1336. Effect of Carbutamide on Serum-cholesterol Level in Diabetes Mellitus

I. B. MUNRO and D. MURRAY. *Lancet* [Lancet] 2, 1083-1084, Nov. 24, 1956. 2 figs.

In a clinical trial of carbutamide ("BZ 55") in 6 cases of diabetes mellitus at the Victoria Infirmary, Glasgow, it was noticed that the serum cholesterol level tended to fall during the first few days of therapy in some cases, returning to the original level later. Of the 6 cases, 4 showed this effect, and 2 of the cases are described. In the first case the serum cholesterol level fell from 345 to 305 mg. per 100 ml.; in the second, from 300 to 200 mg. per 100 ml. Giving insulin alone did not cause such a reduction. A similar change in serum cholesterol value did not occur in 2 non-diabetic subjects given carbutamide in the same dosage.

C. L. Cope

1337. Effects of Sulfonylurea Drugs in Hospitalized Diabetic Patients

H. L. WILDBERGER and H. T. RICKETTS. *Journal of the American Medical Association* [J. Amer. med. Ass.] 162, 1045-1049, Nov. 10, 1956. 5 figs., 21 refs.

The effect of carbutamide and tolbutamide on the sugar levels in blood and urine of healthy subjects and diabetics is discussed in this paper from the University of Chicago. In 11 healthy subjects blood was obtained fasting and then at 2-hourly intervals for 8 hours; at each interval 200 ml. of milk was administered. Several days later the procedure was repeated except that 2 g. of carbutamide was given by mouth before the first milk feed. After the lapse of a week the experiment was repeated with tolbutamide instead of carbutamide. In 10 of the 11 subjects the fall in the blood sugar level in response to one or both drugs exceeded 15 mg. per 100 ml.; in one subject neither drug had any effect on the blood sugar level. No significant difference between the effects of the two drugs was observed.

In 7 patients with diabetes of varying duration and severity the capillary blood sugar level was determined 4 times daily (fasting and 3 to 4 hours after each meal) and the 24-hour urinary excretion of glucose was estimated, the diet of these 7 patients being kept constant at a level which maintained weight. In some patients insulin was not completely discontinued, but the dose was reduced until glycosuria and hyperglycaemia appeared. Administration of the two drugs was started only when the sugar levels in blood and urine were well stabilized or showing a tendency to increase. An excellent therapeutic result was obtained in one case only; in 3 cases there was a partial response, while in 3 (including one in which adrenalectomy had been performed) there was no response at all. Symptomless leucopenia occurred in 2 cases. Crystalluria was not observed.

Denis Abelson

The Rheumatic Diseases

1338. Clinical Experience with a Combination of Aspirin and Prednisolone in Low Dosage in Rheumatic Diseases. (Esperienze cliniche con l'associazione acido acetilsalicilico prednisolone a piccole dosi in malattie reumatiche)

T. GALLI and S. SOLARI. *Minerva medica* [Minerva med. (Torino)] 2, 1611-1613, Nov. 17, 1956.

In a study carried out at Sampierdarena Municipal Hospital, Genoa, the authors have compared the therapeutic value of a combination of 325 mg. of acetylsalicylic acid, 0.5 mg. of prednisolone, and 50 mg. of ascorbic acid given in tablet form with that of cortisone and acetylsalicylic acid given separately in the treatment of rheumatic disorders.

In one case of recent acute rheumatic fever and 4 cases of active rheumatic fever of long standing or in relapse which were treated with 6 to 12 tablets daily there was relief of the clinical condition within 3 weeks and no side-effects were seen. The combination was then tried as the sole medicament on 5 patients with moderate rheumatoid arthritis; all 5 improved when given 6 tablets daily for 3 months, although therapy had to be interrupted for a week in one case because of gastric upset.

In 10 further patients with rheumatoid arthritis treated with 3 to 6 tablets daily according to their clinical requirements for 2 to 3 months in addition to gold therapy [dosage not stated] the results during a 6-month period of observation have been good. In 2 cases expected exacerbations following gold injections were apparently suppressed by the tablets. Of the last 5 rheumatoid arthritic patients, who were being treated with cortisone, 3 improved after receiving 6 of the tablets daily for one month instead of the cortisone; the other 2 patients relapsed.

In the treatment of other conditions 10 patients with acute osteoarthritis of the knees with effusion improved on taking 6 tablets daily for 10 to 20 days; 3 patients with lumbar osteoarthritis were relieved after taking 6 tablets daily for 6 days, and one patient with sciatica was relieved after 10 days of the same dosage, but another was not improved. Lastly 20 patients with fibrositis responded to 6 tablets daily given for 4 to 6 days.

It is considered that the side-effects of prednisolone and acetylsalicylic acid are minimized when they are given in combination and there even appeared to be a synergism between these two components of the tablets.

G. H. Blair

1339. The Radicular Syndrome and "Low Back Pain". (Syndrome radicaire et "low-back-pain")

P. R. M. J. HANRAETS. *Folia psychiatrica, neurologica et neurochirurgica Neerlandica* [Folia psychiat. (Amst.)] 59, 599-612, Dec., 1956. 11 refs.

ACUTE RHEUMATISM

1340. The Treatment of Rheumatic Carditis with ACTH and Its Effects on the Blood Content of Proteins, Hormones, and Hyaluronidase. (Лечение АКТГ больных с кардиальной формой ревматизма и изменения при этом содержания белков, гормонов и гиалуронидазы в крови)

G. E. ПЕРЧИКОВА. *Проблемы Эндокринологии и Гормонотерапии* [Probl. Endokr. Gormonoter.] 2, 20-25, No. 6, Nov.-Dec., 1956. 3 figs., 4 refs.

During the past 3 years 60 patients suffering from cardiac rheumatism have been treated with ACTH (corticotrophin) at the Institute of Therapeutics (Academy of Medical Sciences), Moscow. In 20 cases there was no established cardiac lesion, the majority of these patients undergoing their first attack of rheumatism. The other 40 patients had an established valvular lesion, which in some cases was causing circulatory disturbances. All had a recurrence of the rheumatism. In addition to routine investigations the blood histamine and hyaluronidase levels, the serum protein pattern, and the blood and urinary levels of steroid hormones were estimated before, during, and after treatment. ACTH was given on the 2nd or 3rd day after admission for a period of 4 to 6 weeks in an initial dose of 60 mg. per 24 hours, which was gradually decreased to 10 mg. per 24 hours. The total dose ranged from 700 to 1,000 mg.

Patients in their first attack of rheumatic fever responded to the treatment rapidly and satisfactorily, and no toxic effects were seen. During the period of follow-up (1 to 3 years) only one patient developed a permanent cardiac lesion (mitral incompetence), while the rheumatism recurred in 2 cases. Patients with established rheumatic lesions did considerably less well, however, a satisfactory result being obtained in only 22, no improvement being noted in 18. Toxic reactions, particularly oedema, were frequent, and there was recurrence of the rheumatism in 8 cases during the period of observation. The hyaluronidase and histamine content of the blood was raised in the majority of patients in the acute stage, but tended to return to normal levels as the result of ACTH administration, especially in patients who improved clinically. ACTH therapy also caused a fall in the serum γ - and α_2 -globulin levels when these were originally raised. In all the patients investigated the administration of ACTH caused an increase in the blood and urinary levels of adrenocortical steroids.

In comparing the results of ACTH therapy with those of the usual antirheumatic substances the author considers that ACTH is more rapid in action and more complete in effect, resulting in fewer recurrences, but it would appear to the author to be unsuitable for the treatment of patients with established rheumatic cardiac lesions.

Marcel Malden

1341. Discrepancies in the Erythrocyte-sedimentation Test in Rheumatic Fever

W. D. ALEXANDER and M. M. ANDREWS. *Lancet* [Lancet] 1, 240-242, Feb. 2, 1957. 4 refs.

The authors have studied the reproducibility of the erythrocyte sedimentation rate (E.S.R.) in 60 patients with rheumatic fever, the E.S.R. being determined by two methods simultaneously, each in duplicate—that of Westergren and a similar method in which heparinized blood was used instead of citrated blood. Blood for all tests was collected at one venepuncture, and the tubes were set up within an hour under identical conditions. The E.S.R. was read at the end of an hour. The packed cell volume and the plasma fibrinogen level were also determined on the heparinized blood samples.

No abnormality of the sedimentation process itself was noted. Discrepancies between a pair of tubes were common with both methods, especially at the initial blood examination—that is, before treatment—in cases of acute rheumatic fever. The average arithmetical difference between the readings of duplicate tubes containing heparinized blood was 7.8 mm. and of tubes containing citrated blood 1.3 mm. With clinical improvement and a fall in the plasma fibrinogen level discrepancies became smaller and less numerous. Discrepancies of more than 20 mm. were noted in 13 instances with heparinized blood and in one instance with citrated blood. The authors conclude that in following the course of rheumatic fever the E.S.R. with heparinized blood may be seriously misleading.

David Friedberg

1342. Group A Beta Hemolytic Streptococci in Relation to Rheumatic Fever. Study of School Children in Miami, Fla.

M. S. SASLAW and M. M. STREITFELD. *A.M.A. Journal of Diseases of Children* [A.M.A. J. Dis. Child.] 92, 550-557, Dec., 1956. 2 figs., 16 refs.

Previous investigations have shown that in the U.S.A. the incidence of rheumatic heart disease in children is directly correlated with latitude, ranging from 3 cases per 1,000 children at 25 degrees N. (Florida) to 45 per 1,000 at 45 degrees N. (Wyoming). At the National Children's Cardiac Hospital (University of Miami School of Medicine), Florida, the authors have investigated the characteristics of β -haemolytic (Group-A) streptococcal infections in the school-children of Miami in an attempt to explain the low incidence of rheumatic fever in the South. A total of 6,400 cultures were prepared from throat swabs monthly for 2½ years from 740 children aged 6 to 9, and cultures for Group-A streptococci from single swabs from another 1,200 children.

The over-all monthly incidence of positive cultures was 11.2%, and 25 to 40% of the children harboured Group-A streptococci at least once during any one school year (8 months). The distribution of streptococcal types was similar to that in other reported studies. Anti-streptolysin O (A.S.O.) titres were determined on 1,400 blood samples from the children. Higher titres were found in children whose throats had yielded Group-A streptococci than in those with negative results. In serial A.S.O. titre determinations a significant rise (2 or

more tubes) was found in 50.7% of those with positive cultures. Only 8.6% of bacteriologically negative children showed a significant rise in A.S.O. titre.

From these results it is concluded that about 40% of children in this age group in Miami harbour Group-A streptococci in the throat at some time during each school year, and that half of these, that is, those showing a rise in A.S.O. titre, must be regarded as cases of true streptococcal infection of the upper respiratory tract. On the basis of the postulate commonly accepted in the U.S.A. that 3% of untreated Group-A infections proceed to rheumatic fever, the administrative area in Florida studied should have yielded 212 cases of rheumatic fever among the 35,350 school children at risk in the relevant period. In fact no cases occurred in this area and only 73 in the whole State. The authors discuss the definition of streptococcal infection, and deduce the importance of climatic and environmental factors in the aetiology of rheumatic fever.

E. J. Holborow

1343. Response by Antibodies to Tissue Antigens in the Course of Rheumatic Fever

V. WAGNER and V. REJHOLEC. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 15, 364-372, Dec., 1956. 3 figs., 35 refs.

Pathogenic anaphylactic phenomena in rheumatic fever based on the development of cyto-allergy and the development of auto-organo-antibodies have been postulated and the hypothesis investigated for some years. The techniques of investigation are difficult and attempts at conclusive corroboration not always successful. This paper from Charles University, Plzen, and the Research Institute of Rheumatic Diseases and Charles University, Prague, deals with the verification in closely controlled experiments of the presence of auto-antibodies to various organ antigens in the course of rheumatic fever and the relationship of the antibody titres to various clinical features of the disease. The technique of the preparation of organ antigens adsorbed to nitrocellulose collodion particles is fully described. Antigens were prepared of the myocardium, connective tissue of the heart and valves, subcutaneous tissue, skin, and joint capsule. Frequent serial agglutination estimations were made in 42 cases of rheumatic fever in 38 patients.

Auto-antibodies were found at least once in the blood of every patient. At the initial examination 81% were found to have antibody to at least one type of organ antigen. The titre level was statistically related to the amount of treatment given before entry to hospital, the higher titres (1:16 or more) being observed in untreated cases or those inadequately treated with salicylates or amidopyrine. In most cases (80 to 95%) in which there was an antibody to one antigen, there were also antibodies to the other antigens tested, while the proportion of patients with consistently negative reactions to any one antigen ranged from 2.6% (for antibody to subcutaneous tissue) to 29.8% (for antibody to joint capsule). The correlation between the presence of antibody, whether of all five types or of only the anti-myocardial and anti-valvular types, with the signs of cardiac damage was shown to be statistically significant. Similarly "re-infection in the course of the disease" produced a rise

in agglutinating titre of significance. No antibody was ever found in the "very numerous" control group of healthy subjects. [The very high proportion of cases giving agglutination titres against all types of antigen would seem to be of importance in the assessment of the basic anaphylactic hypothesis and of the significance of organ specificity.]

Harry Coke

CHRONIC RHEUMATISM

1344. Psoriasis and Arthritis

V. WRIGHT. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 15, 348-356, Dec., 1956. 7 figs., 36 refs.

Rheumatoid arthritis and psoriasis, occurring singly, are commoner in females than in males; erosive arthritis in association with psoriasis is, however, relatively common in males. In this paper a study is reported of 34 patients (18 males and 16 females) suffering from both arthritis and psoriasis. Usually the psoriasis preceded the onset of arthritis. Nail lesions were often detected, changes in the nails including thickening, ridging, pitting, and separation from the subungual bed. The distal interphalangeal joints were frequently the site of the initial attack of joint disease. The finger tips were spade-like, with considerable swelling of the distal joint. Subcutaneous nodules combined with effusions into the extensor tendon sheaths were present in only one case. Complete remission of the arthritis was recorded in 17 cases.

C-reactive protein was found in the serum of 15 patients, but the differential agglutination test yielded positive results in only 2. The serum cholesterol level was raised in 9 patients, in 3 of whom it was over 300 mg. per 100 ml. The serum alkaline-phosphatase activity, taken as a measure of the amount of bone destruction, was increased in most cases.

The findings in this series of cases were compared with those in 55 patients with rheumatoid arthritis giving a positive reaction to the differential agglutination test and in 310 patients suffering from psoriasis alone. In patients with the syndrome of psoriasis and erosive arthritis there was apparently less anaemia, the erythrocyte sedimentation rate was lower, and there was less tendency to leucocytosis than in the patients in the other two groups. The association of psoriasis with osteoarthritis, gout, or rheumatic fever was considered to be fortuitous.

A. Garland

[A second paper dealing with the same series of cases primarily from the dermatological aspect was published in *British Journal of Dermatology* for January, 1957. See Abstract 1386.—EDITOR.]

1345. Intermittent Hydrarthrosis

S. MATTINGLY. *British Medical Journal* [Brit. med. J.] 1, 139-143, Jan. 19, 1957. 2 figs., 38 refs.

Although intermittent hydrarthrosis is not rare, fewer than 180 cases have been reported. An analysis of 101 of these shows that the sex incidence is about equal (52 males and 49 females) and that age at onset is usually 20 to 50 years. The author describes 3 additional cases,

all in females. In the first case intermittent swelling of the right knee started at the age of 41 years and recurred at intervals of 9 to 13 days, the attacks bearing no relation to menstruation. The results of laboratory investigations were normal. A course of gold injections was followed by a remission which has lasted 5 years. In the second case symptoms were first noted at the age of 27 years, there being painless swelling of the right knee. Thereafter the patient experienced pain and swelling of both knees at intervals of 2 to 4 weeks for some years, apart from short remissions following illnesses. Again the results of laboratory tests were normal, and the joint fluid was sterile. Rest in bed and corticotrophin injections did not affect the periodicity of the effusions. A remission which followed radiotherapy has now lasted for 4 years. The patient in the third case had had prolonged rest in bed at the age of 19 years and again at the age of 27 years for acute "rheumatism" in the legs. When she was 45 intermittent hydrarthrosis developed, recurring in both knees every 8 days and accompanied by fever. The erythrocyte sedimentation rate was increased and radiographs of the knees showed some osteoporosis. Rest in bed and antihistamine drugs appeared to give temporary relief. The effusions suddenly ceased when the patient was 48, but intermittent swelling of the eyelids was noted for some months after this. The remission has now lasted for 5 years.

The cases described in the literature fall into two groups—those in which the periodic effusions were not accompanied by any evidence of joint damage and those in which a rheumatic disorder was already present. In his discussion the author shows that none of the many causes postulated for this condition or the many treatments advocated has any very firm basis. Spontaneous remissions and relapses are common. He considers that gold therapy is worth further trial, and that radiotherapy and synovectomy may also produce remissions.

B. E. W. Mace

1346. Laboratory Aids in Steroid Therapy

J. H. GLYN. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 15, 338-345, Dec., 1956. 2 figs., 32 refs.

In studies carried out at the Middlesex Hospital, London, the author has attempted to assess the activity of chronic rheumatic disease before and after steroid therapy with cortisone and its analogues by performing repeated estimations of serum levels of hexosamine, Winzler mucoprotein, and total protein-bound polysaccharides, and by determining the erythrocyte sedimentation rate, the plasma fibrinogen and C-reactive protein levels, and serum resorcin turbidity. Some of the tests were applied to 70 patients suffering from various collagen vascular diseases, and all of them serially in 8 cases which were clinically assessed (a) subjectively, the patient's over-all impression being recorded, and (b) objectively by measuring the swelling, tenderness, and mobility of the most affected joints. It is these last 8 cases which are reported here and which form the basis of the author's conclusions, as follows. (1) All the indices were consistently raised and roughly related to activity of the disease in active rheumatoid arthritis,

but there were very few abnormal readings in normal control subjects. (2) Cortisone and hydrocortisone consistently reduced the raised indices towards normal, cessation or reversal of the downward trend implying inadequate dosage of the steroids. (3) The tests were not reliable enough in individual cases to permit of their being recommended for routine clinical use. (4) The mean pre-treatment serum levels of hexosamine and mucoprotein were high and tended to remain above normal, even when large doses of steroids were given. These two indices may therefore be of value in distinguishing between true remission of the disease and mere repression of the symptoms and signs by the drug. Support for this suggestion was found in the observation that these two indices, together with the serum total protein-bound polysaccharide level, were unaffected by evanescent fluctuations in the activity of the disease, in contrast to the other serum values studied. It is postulated that both hexosamine and mucoprotein are derived from the glycoproteins of intercellular ground substance by depolymerization, and that the corticosteroids probably act by inhibiting this depolymerization.

M. Kendal

1347. **The Changing Pattern of Rheumatic Heart Disease. The Experience in New York City Department of Health Cardiac Consultation Clinics, 1943 to 1953** L. KUSKIN and M. SIEGEL. *Journal of Pediatrics* [J. Pediat.] 49, 574-582, Nov., 1956. 3 figs., 22 refs.

An analysis is presented of the diagnoses reached in 65,044 examinations of children at the New York Cardiac Consultation Service Clinics during the period 1943 to 1953 inclusive, the object being to determine whether there had been a change in the relative incidence of organic heart disease following rheumatic fever. Some 80% were first examinations, but the percentage of re-examinations rose from an average of 14 during the first half of the period to 26 during the second. The cases seen in the clinics each year were divided into 3 broad diagnostic groups—non-cardiac, possible heart disease, and organic or potential heart disease. There was a sharp rise in the percentage of non-cardiac cases from 1951 onwards, which is considered to be due partly to the increase in the number of re-examinations and partly to a change in the type of case referred.

Patients with "organic or potential heart disease" were again divided into 4 sub-groups as follows: (1) rheumatic heart disease—history of rheumatic fever with positive heart signs; (2) potential heart disease—history of rheumatic fever but no signs of heart disease; (3) unknown heart disease—organic heart disease of rheumatic type without a history of rheumatic fever; and (4) congenital heart disease. In 1943 60% of the children with a history of rheumatic fever had detectable heart disease when examined. This percentage steadily fell to about 30 in 1948, and has remained at the lower level ever since. The authors point out that this decrease in rheumatic heart disease is in keeping with the findings of other investigators. They also note that 86% of the patients with a history of rheumatic fever were referred to the clinics after the first attack. The incidence of

organic heart disease was about 35% higher in those with a history of more than one attack of rheumatic fever than in those who had had only one known attack.

E. H. Johnson

1348. **Studies of Hyaluronic Acid in Rheumatoid Arthritis**

N. EGELIUS, E. JONSSON, and L. SUNDBLAD. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 15, 357-363, Dec., 1956. 4 figs., 11 refs.

The hyaluronic acid molecule polymerizes to a considerable extent and, because of its complexity, this produces a large micelle influencing the viscosity of the fluid in which it is maintained. A relatively high degree of polymerization of the contained hyaluronic acid is typical of normal or uncomplicated traumatic synovial fluid. Depolymerization is especially noted in rheumatoid arthritis and has been previously reported by the present authors and many others.

In the hope that determination of the degree of polymerization might provide a convenient objective record of the effects of treatment in joint diseases, samples of joint fluid from 119 cases of rheumatoid arthritis and osteoarthritis have been studied at Södersjukhuset, Stockholm, and the "anomalous viscosity" (A), which is regarded as a sensitive index of the degree of polymerization, estimated. Details of the method have been described elsewhere (Sundblad, *Scand. J. clin. Lab. Invest.*, 1954, 6, 288; *Abstracts of World Medicine*, 1955, 18, 63). In normal joint fluids the values (given as $A \times 10^3$) have a range of 80 to 100. Fluid from affected joints in cases of rheumatoid arthritis before treatment gave an average value of 51.4. The changes in viscosity appear to be localized to the affected joints, since fluid from clinically normal joints in the same patient gives normal figures. No correlation of the degree of hyaluronic acid changes with the clinical activity of the disease was found, nor with the results of a considerable number of radiological and laboratory investigations. The viscosity values tended to be lower in early cases, in cases without bone destruction, and in younger patients.

After treatment by the intra-articular injection of hydrocortisone acetate in 30 cases of rheumatoid arthritis and of hydrocortisone tributylacetate in 11 cases the average values of $A \times 10^3$ showed a statistically significant change towards normal. There was no significant difference in effect between these two drugs, nor in the duration of their effect, and there was no difference between the biochemical responses to doses of 25 and 50 mg. The effect of hydrocortisone on the state of polymerization of hyaluronic acid was unaffected by the simultaneous administration of either hyaluronidase or polyphoretin phosphate, a hyaluronidase inhibitor (in one case each). It is therefore stated that "it seemed unlikely that the action of hydrocortisone on the hyaluronic acid was mediated by any influence on the hyaluronidase factors". [Nevertheless the direct introduction of hyaluronidase enzyme would be expected to have some depolymerizing effect. This would suggest that the hydrocortisone might itself inhibit hyaluronidase. The authors have, however, previously reported a decrease in hyaluronidase inhibitor as a result of hydro-

cortisone administration. These reactions are evidently complicated and themselves "anomalous", and some further investigation *in vitro* might be well worth while.]

Only slight changes in the anomalous viscosity were found in 3 cases of rheumatoid arthritis treated with hydrocortisone by mouth (up to 80 mg. daily), with comparatively slight clinical response. On the other hand treatment with prednisone, 20 to 30 mg. daily, by mouth in 2 cases gave a good clinical response and increases in $A \times 10^3$ of 23% and 43% respectively. Little or no change in anomalous viscosity was obtained after the intra-articular injection of cortisone (50 mg.) in 5 cases or of phenylbutazone (600 mg.) in 10 cases, or after treatment with salicylic acid (5 to 6 g. daily) by mouth in 3 cases, with various forms of physiotherapy in 8 cases, or with x-ray therapy in 3 cases.

The authors conclude that this method "provides a convenient method of recording objectively the effects of treatment of rheumatoid arthritis". *Harry Coke*

1349. Rheumatoid Arthritis with Chronic Leg Ulceration
J. H. ALLISON and F. R. BETTLEY. *Lancet [Lancet]* 1, 288-290, Feb. 9, 1957. 2 refs.

Unusually chronic ulceration of the leg associated with rheumatoid arthritis was seen in 6 patients (3 males and 3 females) at the Middlesex Hospital, London, the duration of the rheumatoid arthritis varying from 6 to 20 years. All the patients had had at least one course of gold injections and some had received phenylbutazone as well. There was a history of dermatitis following gold therapy in 4 cases. Subcutaneous nodules were noted at some stage of the disease in all cases. The ulcers were single or multiple, indolent, always on the lower limbs, and frequently about the ankle-joints. There was a history of painful induration which in the course of a week or two broke down to give a punched-out ulcer. There was no evidence of venous stasis in the affected legs. Histologically, the margin of the ulcer was formed by vascular granulation tissue, and there were necrotic bands of tissue in the base; occasionally giant cells were seen. The ulcers were very slow to heal even with rest in bed. Skin grafting was tried and failed in 3 cases, while in 3 recovery followed steroid therapy. L.E. cells were present in the peripheral blood in 4 cases.

Discussing the significance of these findings the authors express the view that the ulcers are manifestations of disseminated lupus erythematosus, which is closely related to rheumatoid arthritis. *William Hughes*

1350. Local Injection of Hydrocortisone and Procaine in Osteo-arthritis of the Hip Joint

V. M. LEVEAUX and C. E. QUIN. *Annals of the Rheumatic Diseases [Ann. rheum. Dis.]* 15, 330-337, Dec., 1956. 4 figs., 5 refs.

The authors report, from the Middlesex Hospital, London, the results of injecting 30 osteoarthritic hip-joints with either 5 ml. of 2% procaine (15 cases) or 5 ml. of 2% procaine containing 50 mg. of hydrocortisone (15 cases). In making the injection a caudo-lateral approach was used. The condition in the two groups, as assessed for severity on the clinical and radio-

logical findings, was found to be similar. Improvement was judged by degree of relief of pain and the time taken to walk a given distance, the patients being examined before and at intervals after the injections. When any effects had worn off the injections were repeated with the preparation not previously given.

The first injection produced a similar degree of pain relief, namely, slight to marked, in 11 patients in each group, but the duration of relief was longer after procaine (mean 3.07 weeks per patient) than after the combined injection (1.6 weeks); there was a similar difference in improvement in walking ability in the two groups. These results were in marked contrast to those of the second injection, however, which produced improvement in only one patient and deterioration in 10 of those receiving procaine alone, whereas the combined injection resulted in improvement in 13 cases and aggravation in only one, the average duration of improvement being 2.5 weeks. The explanation of this marked difference is not clear, but the authors state that the psychological response of the patients to a new and rather dramatic form of treatment cannot be overlooked; repeated injections would probably be required in order to arrive at an accurate assessment. The patients were not aware which drugs were being injected.

The authors conclude that combined injections of hydrocortisone and procaine are of definite palliative benefit in osteoarthritis of the hip-joint, whereas procaine alone often aggravates the condition. *M. Kendal*

1351. Studies in Osteo-arthritis Using Intra-articular Temperature Response to Injection of Hydrocortisone Acetate and Prednisone

J. L. HOLLANDER and R. MOORE. *Annals of the Rheumatic Diseases [Ann. rheum. Dis.]* 15, 320-326, Dec., 1956. 2 figs., 10 refs.

At the University of Pennsylvania Hospital, Philadelphia, the authors have studied the effect of local injections of steroids on the intra-articular temperature of the knee-joint in 21 cases of osteoarthritis, 5 similar cases acting as controls. The temperature was recorded by a thermo-couple passed through the needle into the joint, any fluid present in the joint being aspirated beforehand. In 18 cases the injection consisted of 37.5 mg. of hydrocortisone acetate in 1.5 ml. solution, and in 3 cases (all of generalized osteoarthritis) of 15 mg. of prednisone in 1.5 ml. solution. Only one injection was given in each study, and the temperature was recorded initially and again after 24 and 48 hours and after 5 days.

In the 7 control joints (5 patients) the initial temperature was between 31.5° and 36° C., being above 33° C. (the upper limit of normal) in 4 cases. After 24 hours there was a variation of up to 0.4° C., but thereafter only slight or no change. The synovial fluid from 5 of these joints showed no significant change in viscosity (which was characteristically high), mucin clot formation, or cell count (predominantly mononuclear cells). Insertion of the needle produced partial relief of the pain and stiffness in 6 of the knees which lasted for 3 or 4 days. In all the joints receiving injection of steroids the initial intra-articular temperature was 33° C. or over, the range

being 33.0° to 36.3° C. After the injection the temperature rose by 0.5° to 2.1° C., usually within 24 hours, but in most of the cases had returned to near the original level at the end of 5 days. In the 5 cases of osteoarthritis of the knee joints associated with obesity, however, the temperature either showed no change or fell, with a subsequent tendency to revert to the original level. The only change produced in the synovial fluid (examined in 7 cases) was an elevation of the leucocyte count. Nearly all the patients experienced relief of pain and stiffness for periods varying from 7 to 90 days, the relief being described as complete in most cases.

The authors have thus confirmed the elevated joint temperature previously described in osteoarthritis, and that the temperature is further raised in some types of osteoarthritis by the intra-articular injection of steroids (in contrast to rheumatoid arthritis, in which it falls). There were no correlated changes in the synovial fluid, however, and no direct relation between the temperature change and relief of symptoms. They suggest the possibility that changes in intra-articular temperature may reflect the amount of blood flow to the joint, but trauma from the needle and transient irritation effects of the steroid may complicate the picture.

M. Kendal

COLLAGEN DISEASES

1352. Dermatomyositis. Unusual Features, Complications, and Treatment

H. B. CHRISTIANSON, L. A. BRUNSTING, and H. O. PERRY. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] 74, 581-589, Dec., 1956. 21 refs.

The authors have reviewed the records of 270 patients with classic dermatomyositis seen at the Mayo Clinic between 1916 and 1954. Of these patients 179 were female and 91 male, a ratio of very nearly 2:1. There was a family history of the disease in only one case. Some type of malignant disease accompanied the dermatomyositis in 18 cases (6.7%). Although it has been claimed that the incidence of malignant disease is unduly high in patients with dermatomyositis, the authors were satisfied that in their cases the malignancy was incidental, the age range of the 18 patients being 40 to 72 (mean 55) years.

Cushing's syndrome was observed in two young female patients and it appeared to have an ameliorating effect on the dermatomyositis. The clot test for lupus erythematosus gave a positive result in 2 cases, and in a further 2 patients the skin eruption had the characteristics of pityriasis rubra pilaris. Dysphagia of some degree occurred in 60% of the patients and an [unstated] number of cases of abdominal pain, gastro-intestinal bleeding, and perforation of multiple gastric ulcers also occurred. Osteoporosis was recorded in 30 patients and calcinosis in 28, but there did not appear to be an obvious correlation between these two complications; calcinosis was most frequent in patients under 16 years of age, of whom 29.1% were affected.

In recent years 62 of the patients have been treated with cortisone, of whom 28 improved, 9 obtaining a

permanent remission. In 15 cases the disease appeared to have been uninfluenced by treatment, and 11 patients died despite the treatment. Complications of cortisone therapy included hypertension, diabetes mellitus, and osteoporosis. In view of the short periods of treatment with cortisone the authors are unwilling to draw hasty conclusions, but they consider that cortisone treatment was of definite value, and in some of their cases was life-saving.

J. N. Harris-Jones

1353. Localized Scleroderma. A Clinical Study of Two Hundred Thirty-five Cases

H. B. CHRISTIANSON, C. S. DORSEY, P. A. O'LEARY, and R. R. KIERLAND. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] 74, 629-639, Dec., 1956. 3 figs., 9 refs.

In this report from the Mayo Clinic are reviewed the case records of 235 patients with localized scleroderma seen at the Clinic during the period 1923-54. They were divided into two groups: (1) those with linear lesions and plaques of morphea (191 cases); and (2) those with generalized bilateral, symmetrical morphea (44 cases). Of the 191 patients in Group 1, 146 were female, a ratio of females to males of 3:1. The histories showed that the onset of the illness was frequently associated with trauma, infection, surgical operation, pregnancy, the menarche, or the menopause. A table showing the location and distribution of the lesions is given. Arthralgia, commonly limited to the side of the skin lesion, occurred in 44% of this group. Raynaud's phenomenon, usually involving the ipsilateral limb, was recorded in 8 cases, migraine in 31, and epilepsy in 6. A large range of skeletal abnormalities mostly involving the vertebral column were observed and are tabulated. Residual pigmentation was noted in 82 patients, and facial hemiatrophy in 38.

Individual histories (with photographs) from both groups of cases are given.

J. N. Harris-Jones

1354. The Vascular Lesion in Viscerocutaneous Collagenosis

A. A. SHARP. *British Journal of Dermatology* [*Brit. J. Derm.*] 69, 50-56, Feb., 1957. 9 figs., 24 refs.

The author, from the Royal Victoria Infirmary, Newcastle upon Tyne, reports 3 cases in which careful study of serial sections post mortem suggested a common vascular aetiology, the clinical and gross pathological findings being respectively of systemic lupus erythematosus, scleroderma, and dermatomyositis. Small arteries and arterioles of skin and of internal organs showed hyaline or granular material partly or totally occluding the lumen. It was adherent to endothelium, contained round cells and polymorphonuclear leucocytes, and appeared later to be covered by endothelium so as to lie deep to the intima. Further study suggested conversion of this material into fibrous thickening. The author considers, in view of these findings, that there is much to be gained by adopting the term "viscerocutaneous collagenosis" to include a wide range of clinical entities provided "we could be sure what the term 'collagenosis' implies".

John T. Ingram

Physical Medicine

1355. Diagnostic Use of Ultrasound

J. J. WILD and J. M. REID. *British Journal of Physical Medicine* [Brit. J. phys. Med.] 19, 248-257 and 264, Nov., 1956. 15 figs., 19 refs.

At St. Barnabas Hospital, Minneapolis, Minnesota, ultrasonics have been used to investigate the presence of abnormalities in living breast tissue *in situ* and the results compared with the postoperative pathological reports. Ultrasonics have been applied in medical diagnosis only since about 1947. The methods of investigation may be either by transmission of ultrasound waves via the tissues being examined to a receiver on the farther side which measures the amount of energy not absorbed, or by reflection, in which the transmitter and receiver are placed together on the same side and the reflected energy is measured and displayed on a cathode-ray tube. The latter method the authors have named "echography". By moving the transmitter over the tissues, that is, scanning, a "two dimensional echogram" can be produced. The authors include in this paper a review of the scanty literature and describe clearly the physics of ultrasonics.

In the experiments reported a reflection technique was used, the transmitter generating a pulse of 15 megacycles per second with a peak intensity below 70 watts per sq. cm. It has been shown that cancerous tissue returns more sound, and that non-malignant tumour tissue returns less sound, than normal tissue. In studying abnormalities in the female breast the "two dimensional echograms" were examined and a diagnosis made which was later compared with the pathological findings after operation. A correct diagnosis was made in 26 out of 27 cases of malignant disease and 43 out of 50 cases of non-malignant disease. The authors outline further developments envisaged for this diagnostic technique.

J. B. Millard

1356. Ultrasonic Therapy in Rehabilitation. A Supplement to Active Exercise

J. A. MONCUR. *British Journal of Physical Medicine* [Brit. J. phys. Med.] 20, 25-27, Feb., 1957. 8 refs.

At the Bridge of Earn Hospital, Perthshire, a group of 51 patients suffering from such conditions as prolapsed intervertebral disk, osteoarthritis and fracture of the spine, and fractures of the tibia and wrist, who had ceased to respond to active physiotherapy, were selected for treatment with ultrasonic applications to areas of pain. The immediate results were that 8 of the patients became symptomless, 21 improved, and 22 were unaffected. At a follow-up examination 3 months later it was found that on the whole improvement was well maintained.

The author acknowledges the danger of assessing results when control of the investigation is not possible. He suggests that the favourable results were due to

the analgesic effect of "sonation", which enabled these patients to carry out rehabilitative exercises without pain. In his view sonation can achieve this more quickly and more reliably than either infra-red or short-wave irradiation.

W. Tegner

1357. The Influence of Vibration on Temperature and on the Clearance of Radioactive Sodium in Human Subjects

L. H. WISHAM, A. SHAANAN, and W. BIERMAN. *Archives of Physical Medicine and Rehabilitation* [Arch. phys. Med.] 37, 760-765, Dec., 1956. 2 refs.

The authors have investigated the effects of vibration on the temperature of the skin, subcutaneous tissue, and muscle, and on the clearance of sodium from these tissues in a number of out-patients attending the Department of Physical Medicine, Mount Sinai Hospital, New York.

The apparatus for producing vibration consisted essentially of an unbalanced motor suspended within its housing giving frequencies of 1,200 to 12,000 cycles per minute. After stabilization in a room at 75° to 78° F. (24° to 25.6° C.), the temperatures of the skin, subcutaneous tissue, and muscle were recorded with a string-galvanometer thermocouple. Treatment with the vibrator was then given for varying periods and the temperature again recorded; in some cases temperature recordings were made during the treatment. In other experiments 0.05 ml. of isotonic saline containing 1 to 1.5 microcuries of radioactive sodium (²⁴Na) was injected intracutaneously, or 0.1 ml. of the same solution was injected to a depth of 2.5 cm. into the belly of the gastrocnemius muscle, and vibratory treatment given. In the studies of temperature and skin clearance of sodium the measurements were made at the site of contact and also at a distance from the vibrator. The clearance of ²⁴Na from muscle was determined by Geiger counter twice for each subject, these values serving as a control; it was then determined twice after vibration for 30 minutes but before the injection of ²⁴Na, and repeated twice while vibration was given during ²⁴Na clearance, and the results compared.

The detailed results are tabulated. They show that the skin and subcutaneous temperature and clearance of ²⁴Na were increased when in contact with the vibrator by approximate mean values of 2.0° C. and 75% respectively. However, the skin temperature and sodium clearance at a distance from the area of treatment showed little alteration. The temperature and sodium clearance in muscle showed no significant change in any of the experiments.

J. B. Millard

1358. Physical Measures in the Aged

D. L. ROSE, E. B. SHIRES, and W. S. ALYEA. *Journal of the American Medical Association* [J. Amer. med. Ass.] 162, 1524-1526, Dec. 22, 1956. 16 refs.

Neurology and Neurosurgery

1359. **Electroencephalography in the Study of the Pattern of Brain Potentials in Patients with Cerebral Tumours and Injuries.** (Исследование биоэлектрической мозаики коры у больных с опухолями и травмами головного мозга при помощи электроэнцефалоскопии) M. M. LIVANOV, V. M. ANAN'EV, and N. P. BEKHTEREVA. *Журнал Невропатологии и Психиатрии* [Zh. Nevropat. Psikhiat.] 56, 778-790, 1956. 8 figs., 10 refs.

The usefulness of clinical electroencephalography is limited by the impracticability of recording and interpreting the changes in electrical potential occurring in more than 6 to 10 regions of the cortex simultaneously. Methods of toposcropy recently introduced by British workers in this field have partly overcome this difficulty, but their use of separate amplifiers for the different channels makes for extreme complexity of the apparatus.

The present authors describe a system which enables a single amplifying set to monitor, practically simultaneously, 50 channels by means of an electronic scanning device. The electrodes are arranged in five rows of 10 each so as to cover the surface of either one side or both sides of the cranium, the electrical potentials from these being represented by spots of light on a cathode-ray tube which appear in the same spatial relationship to one another as the electrodes. No neutral lead is used, the potential of any one electrode being measured in relation to the average of the whole cortex. The apparatus is so adjusted that in the absence of any electrical activity the spots are all of equal brightness; but when an electro-negative change (excitation) is picked up by one electrode the corresponding spot is caused to become brighter and larger, while conversely an electro-positive change causes diminution in the brightness and size of the spot. The appearances on the cathode-ray tube were also recorded cinematographically.

The characteristics of the changing patterns of brain potentials thus recorded were studied in animals, in the brains of normal human subjects under different forms of stimulation, and in 26 patients with a variety of cerebral lesions, mainly neoplasms. The authors believe that the method may prove of considerable value in the location and diagnosis of cerebral lesions.

Alexander Duddington

1360. **On the So-called Visual Bradykinesia.** (К вопросу о так называемой брадикинезии взора) T. D. DEMIDENKO. *Журнал Невропатологии и Психиатрии* [Zh. Nevropat. Psikhiat.] 56, 882-883, 1956. 5 refs.

The author describes 2 cases of familial progressive cerebellar atrophy investigated at the Bekhterev Neurological Institute, Leningrad, in which paralysis of conjugate upward deviation of the eyes was associated with the syndrome of "visual bradykinesia" on lateral conjugate movements of the eyes. This syndrome, described

by Davidenkov in 1945, consists in slowness in the movement of the eyeballs on conjugate deviation, which is more marked in some directions than others; the full range of movement is retained.

Previously described cases of paresis of upward ocular movement in cerebellar disease reported in the Russian literature are discussed in relation to the author's cases, particularly in regard to the neurological mechanisms involved, and the fact is noted that visual bradykinesia in one plane associated with paresis of movement in the other has not previously been reported.

Alexander Duddington

1361. **The Pupillary Changes in the Holmes-Adie Syndrome**

G. F. M. RUSSELL. *Journal of Neurology, Neurosurgery and Psychiatry* [J. Neurol. Neurosurg. Psychiat.] 19, 289-296, Nov., 1956. 3 figs., 28 refs.

In clinical practice widely varying abnormalities of the pupil are often grouped under the term Holmes-Adie syndrome. In order to throw further light on the pathogenesis of this condition the author has studied 14 cases of the syndrome seen at the Northern General Hospital, Edinburgh, in 9 of which there was also loss of upper limb deep reflexes, in particular, loss of the triceps jerk. The author emphasizes the resemblance between the pupillary changes in some of these cases and the Argyll Robertson pupil.

In 11 cases the pupil was examined after the performance of stellate ganglion block. This resulted in varying degrees of pupillary constriction, the pupil size approximating that resulting from convergence; the degree of constriction was regarded as a measure of parasympathetic preservation. The rate of pupillary relaxation after convergence was unaffected by stellate block. The application of 3% cocaine hydrochloride and 0.1% adrenaline hydrochloride to the conjunctiva was used as further test of sympathetic function. Cocaine caused dilatation of all pupils which were not already fully dilated, whereas adrenaline had no effect. This led to the conclusion that there was no evidence of any lesion of the sympathetic pathways in cases of tonic pupil. Parasympathetic function was tested by instilling into the conjunctival sac 0.25% eserine, 2.5% methacholine, 1% pilocarpine, and 0.5% homatropine. In response to methacholine 14 out of 19 pupils tested showed constriction. The response to pilocarpine varied from marked sensitivity to no reaction at all.

In agreement with earlier observers the author concludes that the lesion responsible for the tonic pupil in this syndrome must be somewhere along the parasympathetic pathways and he considers that the constant irregularity of the pupils suggests that there is patchy involvement of the short ciliary nerves. As the lesion becomes more severe hypersensitivity to methacholine

decreases, and in such pupils the tonic reaction is slight or absent, probably because little or no acetylcholine is liberated. The considerable clinical variation that is found among tonic pupils seems to depend on the co-existence of varying degrees of paralysis and hypersensitivity.

L. G. Kiloh

1362. The Treatment of Myotonia

L. A. LIVERSEDGE and M. J. D. NEWMAN. *Brain [Brain]* 79, 395-413, Sept., 1956. 10 figs., 7 refs.

Various substances were evaluated in the symptomatic treatment of 10 cases of dystrophia myotonica and one of myotonia congenita at the Manchester Royal Infirmary (University of Manchester). A quantitative method was used to determine the strength of the grip and the duration of myotonia in flexor sublimis digitorum. [For the technical details of this method the original paper should be consulted.] Procainamide and deoxycortone acetate had no apparent effect on either power or myotonia. Cortisone and corticotrophin reduced significantly the duration of myotonia in 8 out of 9 cases; in 3 of these myotonia was abolished. Muscle power was not influenced. The effect of quinine was similar to but less marked than that of cortisone or corticotrophin. The authors consider that treatment with cortisone is indicated only in those cases in which myotonia is the predominant symptom.

J. W. Aldren Turner

BRAIN AND MENINGES

1363. Cough Headache

C. SYMONDS. *Brain [Brain]* 79, 557-568, 1956. 6 refs.

Coughing and actions such as sneezing, straining at stool, laughing, or stooping, which often aggravate headache whatever its cause, may also occasionally provoke it. This liability of coughing to cause immediate and transient pain in the head is not infrequently observed in cases of intracranial tumour, but is then ordinarily associated with the occurrence at other times of headache which is spontaneous and of a different kind. There is, however, a group of patients having the liability to brief, severe pain in the head precipitated by the factors mentioned, and especially by coughing, in whom no evidence of intracranial or cranial disease is to be found. This paper is chiefly concerned with this type of case, but for comparison 6 cases are recorded in which transient severe pain in the head on coughing, sneezing, straining at stool, laughing, or stooping was for a long time the only symptom of organic intracranial disease. These included a posterior fossa meningioma, a cyst of the midbrain, 3 cases of basilar impression from Paget's disease, and one in which the symptom developed after the removal of an acoustic nerve tumour. The mechanism of the pain in these cases is discussed and it is suggested that in some way the increased venous pressure resulting from coughing or similar actions was capable, in the presence of abnormal pressure within the posterior fossa, of causing the headache. A mechanism of pro-

duction similar to that of lumbar-puncture headache is suggested and the possibility of the stretching of pain-sensitive structures is discussed in relation to the observations of surgeons operating under local analgesia.

In contrast, 21 cases are reviewed in which there was a similar production of headache on coughing, but in which there was no evidence of organic intracranial disease, although in few instances was a space-occupying lesion absolutely excluded, mainly because the cough headache was not disabling. There was, however, sufficient evidence that the 21 cases formed a homogeneous group in which the cough headache occurred as a benign symptom. In 9 cases there was eventual recovery and in 6 cases there was substantial improvement at the time of the last observation. In 6 further cases the evidence against progressive intracranial disease was presumptive. It is suggested that a similar mechanism of production of the headache may be at work in cases of benign cough headache as in those cases associated with an intracranial lesion, and that the pain is due to stretching of pain-sensitive structures within the posterior fossa. Some support for this explanation is provided by the observation that in 5 of the 21 cases there was some disturbance of auditory or vestibular function.

J. MacD. Holmes

1364. Cerebral Dominance in Sinistrals

G. ETTLINGER, C. V. JACKSON, and O. L. ZANGWILL. *Brain [Brain]* 79, 569-588, 1956. 4 figs., 15 refs.

It has become clear in recent years that the relationship between handedness and cerebral dominance is far less clear-cut than was formerly supposed. Although the classic rule relating right-handedness and dominance of the left hemisphere has not been seriously challenged, the position with regard to left-handedness has undergone a complete transformation. No longer can it be accepted that right cerebral dominance is the rule in left-handed individuals or that aphasia resulting from a left-sided lesion in a left-handed patient is in any way exceptional.

In this paper from the National Hospital, Queen Square, London, detailed case reports are presented of 10 left-handed patients in whom dysphasia and kindred disturbances were observed in association with unilateral cerebral lesions. The lesion was left-sided in 8 cases and right-sided in 2. Outspoken dysphasic syndromes occurred in 3 cases with left-sided lesions and in one case with a right-sided lesion. In this last case the speech disorder was transitory. One patient with a left-sided lesion showed severe dysgraphia and constructional defects with minimal dysphasia. Minimal dysphasic signs were elicited in 4 cases, 3 with left-sided lesions and one with a right-sided lesion. In one case of left-sided lesion there was no speech disorder whatsoever. Disorders of praxis and body-scheme were present in 3 patients with involvement of the left parietal lobe. One patient with a right parietal lesion presented signs of unilateral neglect and visuo-constructive disorder without appreciable dysphasia. Analysis of the findings indicated consistent left hemispheric dominance for all major functions in 5 cases and probable left hemispheric

dominance in 2. Right hemispheric dominance was indicated, if less certainly, in 2 cases. In one case there was evidence of left hemispheric dominance for praxis and topognosis and right hemispheric dominance for language processes.

The findings are discussed with special reference to the hypothesis of bilateral speech representation in left-handed individuals. It is concluded that "whereas some degree of 'cerebral ambilaterality' may exist in a certain proportion of cases, unilateral representation of speech (usually left, but occasionally right) is the most prevalent form of cerebral organization in sinistrals".

J. MacD. Holmes

1365. Disorders of Laughter Due to Brain Lesions

R. IRONSIDE. *Brain [Brain]* 79, 589-609, 1956. Bibliography.

This paper reviews the present state of knowledge concerning disorders of laughter resulting from focal cerebral lesions. From a study of personal cases and an extensive review of the literature the author concludes that abnormal laughter responses may be due to widely distributed lesions at various neurological levels of the brain.

(1) At the lowest level—as at the highest—involuntary, uncontrollable, and explosive spasms of laughter or weeping occur in pseudo-bulbar and bulbar syndromes which do not conform in degree or duration to emotional feeling and for which an appropriate stimulus may be lacking. They commonly cause embarrassment and distress to the patient. Mental changes and disturbances of consciousness are absent. These spasms occur in patients with lesions of the facio-respiratory and bulbar nuclei and suprasegmental motor tracts; the majority, but not all, show signs of bilateral pyramidal disease. The difficulties of distinguishing between the crude bulbar automatisms of mirthless laughter and emotional lability are seen in this group of cases.

(2) At the intermediate (posterior diencephalic and limbic) level a convulsion of laughter analogous to Jacksonian epilepsy may occur with or without disturbances of consciousness. Laughter may constitute the prodrome or the attack itself. These attacks often resemble temporal-lobe fits. Sudden hypotonia may induce falling. (This group includes "ictus ridendi" in which prolonged laughter ends in hemiplegia, a fit, stupor, or dementia.)

(3) At the highest level (anterior hypothalamic, frontal, and temporal) emotional lability or emotional incontinence is part of a complex mental disorder shown by excited speech or behaviour and giggling. Some mental functions may be stimulated, others paralysed. Here there may be coexistent defects of memory, attention, and perception. Large lesions situated near the midline cause disturbances at this level. There may be associated dysphasia, dyspraxia, hemiplegia, or visual field defects.

These levels, however, are not clearly defined clinically, and it is not the emotional disorder, but rather the associated somatic findings, which will indicate the site of the lesion.

J. MacD. Holmes

1366. The Present-day Position of Treatment of Cerebral Vascular Accidents. (Современное состояние вопроса о лечении мозговых инсультов)

L. S. SOSKIN. *Советская Медицина [Sovetsk. Med.]* 8-18, No. 11, Nov., 1956. 2 figs.

The prognosis of a cerebral vascular accident depends not so much on its site as upon the ischaemia, anoxia, and oedema which result from it. It is therefore essential not merely to locate the lesion, but to determine its nature, that is, whether it is due to thrombosis or haemorrhage. Treatment should then be directed at removing the secondary effects of the lesion.

In cases of thrombosis vasodilator drugs have been employed for this purpose, but in regard to some of these there is no evidence that they produce dilatation of cerebral vessels even though they do cause peripheral dilatation. A number of these substances are appraised. Opinions differ as to the value of anticoagulants and also of operative measures on the stellate ganglion and the cervical sympathetic nerves. Although these methods may achieve a satisfactory result in thrombosis they are not without danger in cases due to haemorrhage. On the other hand ganglion-blocking agents which rapidly lower the blood pressure are contraindicated in thrombosis, whereas they may be useful in haemorrhage. Here chlorpromazine ("largactil") may be given (50 mg. in 2 ml. mixed with 18 ml. of physiological saline) intravenously at the rate of 0.5 ml. every 2 minutes, the blood pressure being checked also every 2 minutes. This treatment should be begun as soon as possible after the haemorrhage.

In general, however, in cerebral haemorrhage conservative measures such as this have not justified themselves. The conception of the surgical removal of cerebral haematomata was put forward over 60 years ago and although much work has been done since then, the problem cannot be regarded as settled. The employment of such treatment in traumatic cases differs from that in spontaneous haemorrhage in that traumatic injuries usually occur in healthy tissues, whereas cerebrovascular accidents occur in atheromatous vessels. Many of the difficulties in the surgery of cerebral haemorrhage have been lightened by modern aids to location of the lesion, such as arteriography, electroencephalography, and the use of radioactive isotopes, and also the use of ganglion-blocking substances for the control of blood pressure and by new methods of ensuring haemostasis; these advances are reviewed by the author. One of the chief unresolved problems is to decide the best moment for surgical intervention. Most authors advise waiting for 48 hours, but some advocate earlier decompression. Again, while German workers on the whole deprecate the use of arteriography in acute vascular incidents, American and French observers have found it has no ill effects, and recommend it as a means of determining early and with accuracy the site of the lesion. The various surgical operations which have been devised for the treatment of lesions at different sites are discussed and briefly described.

The author concludes that whereas conservative measures in the treatment of cerebrovascular incidents due to thrombosis are promising, the results of such

measures in cases due to haemorrhage are so unsuccessful that the problem calls for the increased development of surgical measures in contemporary medical science.

L. Firman-Edwards

1367. Evaluation of Cortisone in the Treatment of Cerebral Infarction

M. DYKEN and P. T. WHITE. *Journal of the American Medical Association [J. Amer. med. Ass.]* **162**, 1531-1534, Dec. 22, 1956. 18 refs.

An investigation of the value of cortisone in the treatment of cerebral infarction is described in this paper from the Indiana University Medical Center and the General Hospital, Indianapolis. A total of 36 patients admitted to hospital with symptoms of cerebral infarction were classified according to the severity of the disability, and then divided into two groups comparable for age, blood pressure, and other essential factors. Both groups received the usual supportive care, and one group (17 patients) were given 300 mg. of cortisone and 3 g. of potassium chloride daily with a low-salt diet, while the remainder (19 patients) received a placebo. The dosage of cortisone in the trial group was gradually reduced after the second day until at 21 days the daily dose was 50 mg., when the drug was withdrawn. There were 13 deaths in the cortisone group and 10 in the control group. The authors conclude that cortisone is of no benefit to patients with cerebrovascular disease; they also state that "there was a trend indicating that cortisone may be a dangerous drug to use in cerebral vascular disease".

[Patients who had transitory symptoms disappearing within a few hours were not included. The method of assessing severity is not very clearly defined. There seems to have been no attempt to determine the precise nature of the vascular lesion by arteriography.]

Hugh Garland

1368. Acute Disseminated Encephalomyelitis and Related Syndromes

H. G. MILLER, J. B. STANTON, and J. L. GIBBONS. *British Medical Journal [Brit. med. J.]* **1**, 668-672, March 23, 1957. 29 refs.

1369. The Ocular Signs of Tumors Involving the Anterior Visual Pathways

F. B. WALSH. *American Journal of Ophthalmology [Amer. J. Ophthal.]* **42**, 347-377, Sept., 1956. 17 figs., 33 refs.

In an analysis of the author's experience at the Johns Hopkins Hospital, Baltimore, of intra- and extra-ocular tumours involving the optic nerve and chiasm, 26 cases of the former are first surveyed. Gliomata were most frequently encountered (17 cases) and of these the great majority were astrocytomata; meningiomata (4 cases) accounted for most of the remainder. Metastatic carcinoma was also observed. Ophthalmoscopically visible involvement of the optic disk was recorded in 3 cases, defective vision in 17 cases, proptosis in 10 cases, optic atrophy in 18 cases (bilateral in 11), papilloedema in 6 cases, generalized neurofibromatosis in 4, and radiologically visible enlargement of the optic foramen in 9. Field changes may be difficult to assess in children, but

when the tumour is chiasmal temporal defects may be found; on the other hand irregular defects or central loss may be observed. The combination of optic atrophy with enlargement of the optic foramen is, of course, diagnostic. Displacement of the globe is not always forwards, and is often downwards; it may be visible in amount, but is not necessarily always present.

Among extra-ocular tumours, meningiomata (31 cases) may affect the visual pathways variably, according to their site. Craniopharyngiomata (23 cases) may be associated with diabetes mellitus, and since optic atrophy is rarely, if ever, an accompaniment of diabetes in young people, their association in such a case should raise a suspicion of tumour. Field loss with persistent retention of normal colour of the disk is another feature which should suggest this condition. Among 55 cases of pituitary tumour affecting the visual pathways there were 46 chromophobe adenomata, 7 eosinophilic adenomata, one carcinoma, and one teratoma. Bitemporal field defects may be considered to be the rule in pituitary tumours, but to find these defects central colour field testing must not be neglected, as it alone may provide the vital clue. Atrophy with a normal coloured disk may also be encountered, but not so frequently as with craniopharyngioma; on the other hand ophthalmoplegia is more common. In 10 cases of malignant nasopharyngeal tumour pain due to 5th nerve involvement associated with deafness due to blocking of the eustachian tube was the outstanding symptom. Multiple unilateral cranial palsies are also highly significant in such cases. Tumours of the third ventricle (5 cases) most frequently have papilloedema as the principal ocular sign, but may produce field defects by pressure on the chiasm or tracts; outstanding features are signs of raised intracranial pressure or of pressure on the hypothalamus.

Two cases of basal arachnoiditis causing visual defect were substantiated by operation, with recovery of vision following the freeing of adhesions. Three cases are reported in which a posterior fossa tumour mimicked a pituitary tumour by presenting with bitemporal field defects, homonymous hemianopia, and enlargement of the sella (due to spread of a meningioma) respectively. Pinealomata, colloid body tumours, and chordomata have also caused defects of the visual fields by pressure.

J. E. M. Ayoub

1370. The Use of Phenolsulphonphthalein in the Clinical Evaluation of Hydrocephalus

E. A. BERING. *Journal of Neurosurgery [J. Neurosurg.]* **13**, 587-595, Nov., 1956. 3 figs., 5 refs.

The author has re-examined the validity of the phenolsulphonphthalein (PSP) test in the light of recent knowledge, since the test was introduced by Dandy and Blackfan for the study of the cerebrospinal-fluid (C.S.F.) system as long ago as 1913. In this paper he analyses the results obtained from the intraventricular injection of PSP in 130 children with communicating and 137 with non-communicating hydrocephalus at the Children's Medical Center, Boston. The lapse of time between the injection of the dye into the ventricles and its appearance

in the lumbar subarachnoid space—the “communication time”—was measured by allowing the lumbar C.S.F. to drip on to a pad moistened with ammonia, a colour change occurring on arrival of the PSP. Urinary excretion of the drug after injection was also measured, the time required for half the dose to be excreted being used as a measure of its turnover.

The author concludes that the absorption of PSP does not truly measure the state of the absorption mechanism of the C.S.F., but measures only the increased volume of the C.S.F. in a very complicated way. It has no real significance in assessing the clinical state of a hydrocephalic patient or in deciding what measures should be carried out in treatment. On the other hand it is a very useful tool in testing for communication between the cerebral ventricles and the lumbar subarachnoid space, particularly when combined with air encephalography. Adequate communication probably exists if the dye appears in the lumbar C.S.F. within 10 minutes of injection into the ventricle. Delay in the appearance of PSP longer than 10 minutes is suggestive of an obstructive lesion, and if the dye does not appear within 18 minutes there is probably an inadequate pathway between the ventricles and spinal subarachnoid space. It is suggested that ventricular air studies should also be performed, as some obstructive cystic lesions of the posterior fossa allow the dye to pass, but not a sufficient volume of C.S.F.

The absorption of PSP is not absolutely altered in hydrocephalus, and its slow urinary excretion is thought to be the result of its dilution in the enlarged ventricle, which apparently has the effect of delaying its absorption. Thus no clinical significance should be given to this slow absorption of PSP in hydrocephalus.

[This is an interesting revaluation of the phenol-sulphonphthalein test. It indicates that the test is of little use as a quantitative measure of cerebrospinal-fluid resorption rates, but has still some value as a test of communication between the ventricles and the spinal subarachnoid space.]

J. MacD. Holmes

EPILEPSY

1371. The Temporal Horn: Its Development, Normal Variations and Changes Associated with Non-expanding Epileptogenic Lesions of the Temporal Lobe. [In English] J. M. VAN BUREN, M. BALDWIN, and E. C. ALVORD. *Acta Radiologica* [Acta radiol. (Stockh.)] 46, 703-718, Dec., 1956. 12 figs., 22 refs.

The effect of non-expanding epileptogenic lesions of the temporal lobe on the outline of the temporal horn as seen at pneumoencephalography was studied at the National Institutes of Health, Bethesda, Maryland, in 41 patients with epilepsy considered to be caused by such a lesion. In all the cases the lesion was subsequently investigated and treated surgically. In the preliminary clinical studies the determination of a “normal” temporal horn proved difficult. Casts of the temporal horn “having the most pleasing appearance” were those in which sufficient space was available

in the horn to allow free entrance of the casting medium. A satisfactory cast could not be obtained of the majority of temporal horns because they were too close to the hippocampus or to the lateral wall, although there was nothing to suggest that these small horns were in any way abnormal. It is therefore suspected that the temporal horns usually depicted in ventricular models are not typical of normal horns. The authors review the embryonic and adult anatomy of the temporal horn as seen in pneumographical studies of the brain. Four normal types are evident in the sagittal projection of the temporal horn, depending on the prominence and position of the collateral eminence. The mechanism of enlargement of the temporal horn is discussed, including enlargement caused by a rotation or displacement of the hippocampus.

Of the 41 cases investigated, in 13 insufficient gas entered the temporal horn for an exact evaluation of its anatomy. In 12 of the remaining 28 cases the measurements of the horn were inconclusive; in 13 cases the lesion was accurately located and in 3 inaccurately located by measurement.

A. Orley

1372. Temporal Lobectomy with Removal of Uncus, Hippocampus, and Amygdala. Results for Psychomotor Epilepsy Three to Nine Years after Operation

A. A. MORRIS. *A.M.A. Archives of Neurology and Psychiatry* [A.M.A. Arch. Neurol. Psychiat.] 76, 479-496, Nov., 1956. 5 figs., 20 refs.

The author reports from Georgetown University School of Medicine, Washington, D.C., the follow-up results after periods of 3 to 9 (average 5) years in 25 male and 11 female patients ranging in age from 14 to 51 years who were subjected to temporal lobectomy for temporal-lobe epilepsy. The indications for operation were disabling and severe psychomotor seizures, with interseizure psychiatric disorder in 18 of the patients, 7 of whom were in institutions. The average length of medical treatment before operation was 14 years, and only those patients were chosen for operation who showed a clear-cut unilateral temporal-lobe focus on electroencephalography. In all cases a full preoperative study, including pneumoencephalography and carotid angiography, was carried out. The operation was a “standard” lobectomy on the affected side in which the anterior 6.5 cm. of the temporal lobe together with the uncus, amygdala, and the anterior parts of the hippocampal and first, second, and third temporal convolutions were removed. Experience had shown that this type of lobectomy could be carried out without concurrent electrocorticography.

The follow-up inquiry revealed that 15 of the patients had had no attacks of any sort since leaving hospital, 12 were much improved, 2 had “fair” results, and 7 showed little or no improvement. One-half of the patients with grand-mal seizures were free from attacks, and two-thirds of those affected were free from disturbing psychiatric complaints, while 30 of the 36 had become economically independent. One patient died in childbirth 4 years after operation. Taking all factors into account the author regards the operation as successful in two-thirds of the patients studied.

J. B. Stanton

1373. Trimethadione: Its Dosage and Toxicity

C. E. WELLS. *A.M.A. Archives of Neurology and Psychiatry* [A.M.A. Arch. Neurol. Psychiat.] 77, 140-155, Feb., 1957. 2 figs., bibliography.

Three cases of severe petit mal seizure disorder are reported in which control was obtained only with the use of relatively massive doses of trimethadione ("tridione"). The pharmacology, indications for use, recommended dosages, and toxicity of trimethadione are reviewed. It is concluded that high dosage of trimethadione is of value in controlling certain cases of petit mal epilepsy and that there is no evidence that such dosages are of greater danger from the standpoint of toxicity than are generally accepted dosages.—[Author's summary.]

1374. Photogenic Epilepsy. (Photogene Epilepsie)

J. A. GANGLBERGER and B. CVETKO. *Wiener Zeitschrift für Nervenheilkunde* [Wien. Z. Nervenheilk.] 13, 22-45, 1956. 6 figs., 34 refs.

Although the interesting condition termed photogenic epilepsy was first described in detail only as recently as 1946 (by Grey Walter *et al.*), the present authors point out that the ancient Greeks must have been aware of it, for they put a low price on slaves who fell off a pedestal when subjected to a flickering light produced, in those days, by the spokes of a revolving wheel held before a small window.

In this communication from the University Neurological Clinic, Vienna, the authors state that the condition is often missed and frequently masquerades under the misnomer of hysteria. The patient himself may be unaware that he suffers from the condition. A careful history is more important than special investigations such as electroencephalography (EEG), and should include searching questions about the effect of intermittent light and shade. Such light effects may be experienced when driving past a row of trees or travelling in a train through an arcade of concrete supports. Some patients are worse in the spring and autumn when the sun is low in the sky and long shadows are more frequently cast. These patients find that they cannot cycle past a row of posts or walk in heavily wooded country without suffering an attack, while the reflection of the sun off the snow often makes skiing impossible. Some patients are affected by the glinting of the sun on the waves of the sea, while others find that the flickering of the picture at the cinema may start an attack.

A total of 79 cases have been collected by the authors, affecting 50 females and 29 males. A clinical account of 9 of the cases is given. The fits produced by the light stimulus varied from myoclonus in some cases to petit mal in others, and less commonly took the form of grand mal. Characteristic changes appeared in the EEG especially after the stimulus of a flickering light. Eight such EEGs are reproduced. One particularly interesting case was that of a girl aged 10 who was described as being difficult at school. She had discovered that she could produce these "absences" in herself by waving her parted fingers rapidly before her eyes and had taken to resorting to this practice whenever she found herself

in a difficult or unpleasant situation. Treatment involves explaining to the patient the nature of the condition, so that he may avoid the conditions likely to bring on attacks. The wearing of red-excluding dark glasses and the administration of drugs of the troxidone type are usually effective. If grand-mal attacks are induced troxidone may have to be combined with other anticonvulsants, such as methylphenobarbitone. The authors discuss some theories of the possible mechanism of production of this reflex type of epilepsy.

G. S. Crockett

SPINAL CORD**1375. Radioactive Vitamin B₁₂ in the Diagnosis of Neurological Disorders**

G. M. BERLYNE, L. A. LIVERSEDGE, and E. W. EMERY. *Lancet* [Lancet] 1, 294-296, Feb. 9, 1957. 4 refs.

The authors, working at Manchester Royal Infirmary, have studied the absorption of vitamin B₁₂ (cyanocobalamin) in 5 normal subjects and in 25 patients with neurological disease of varied aetiology. They utilized the technique of Schilling *et al.* (*J. Lab. clin. Med.*, 1955, 45, 926; *Abstracts of World Medicine*, 1956, 19, 50) in which an oral dose of vitamin B₁₂ labelled with radioactive cobalt (⁵⁶Co) is given and the urinary excretion of this substance during the succeeding 24 hours measured. The oral dose administered contained 3 µg. of vitamin B₁₂ and had an activity of 0.5 µc. The radioactivity of 10 ml. of the 24-hour specimen of urine was compared, using a scintillation counter, with that of 10 ml. of a standard solution of radioactive vitamin B₁₂ prepared by making a 1-in-1,000 dilution of the solution used for oral administration; from this the percentage of tracer substance excreted could be estimated.

Normal subjects were found to excrete between 4 and 7.1% of the ingested dose in 24 hours, whereas in 10 patients with classic subacute combined degeneration of the cord the values ranged from 0.3 to 1.0% (mean 0.6%). The value of this test in the diagnosis of 15 doubtful cases of this disease is illustrated by the detailed description of 6 of these cases in which it enabled a positive diagnosis to be made, which was subsequently confirmed either by the course of events or by the patient's response to treatment. The authors claim that by means of this technique it is possible to confirm or exclude the diagnosis of subacute combined degeneration of the spinal cord with reasonable certainty.

John N. Walton

1376. The Role of Perineurial Sacral Cysts in the Sciatic and Sacrococcygeal Syndromes. A Review of the Literature and Report of 9 Cases

K. H. ABBOTT, R. H. RETTER, and W. H. LEIMBACH. *Journal of Neurosurgery* [J. Neurosurg.] 14, 5-21, Jan., 1957. 14 figs., 18 refs.

Tarlov first described perineurial sacral cysts as presenting a clinical picture similar to that seen in cases of a herniated intervertebral disk. A review of 28 reported cases showed that low back pain and sciatic pain were present in about two-thirds and motor or sensory loss of sciatic distribution in about one-fourth. The present

authors, in this paper from Ohio State University Hospitals, Columbus, report 9 additional cases, in 5 of which it was questioned whether these cysts were necessarily the cause of the sciatic syndrome. It has been shown that in some cases sacral cysts, assumed to be perineurial sacral cysts, are incidental findings at necropsy, myelography, or exploration of the sacral canal; also they may be associated with other lesions—such as lumbar disk herniation or sacral abscess—which are capable in themselves of producing sciatic and sacrococcygeal syndromes. Pressure distension of the affected nerve fibres, with degenerative changes, and pressure against contiguous nerve roots are considered to be the cause of the symptoms in these cases of sacral cyst.

In 3 of the authors' 9 cases symptoms were typical, and in another it was considered possible that the lesion was an intrasacral meningocele. In 4 cases perineurial sacral cysts were associated with other lesions (disk herniation in 3 and a sacral abscess in 1), which were thought to be the cause of the symptoms, while in the remaining case, in which a perineurial sacral cyst was demonstrated radiologically, the symptoms disappeared after myelography. Many of these cysts communicate with the subarachnoid space and may often be diagnosed by myelography. If the contrast medium is left in the spinal canal and radiographs are taken the next day, the medium may then be found to have entered one or more sacral cysts. Erosion of the sacrum with enlargement of the sacral canal in the plain radiograph may be diagnostic. This lesion is one that must be considered in the differential diagnosis of patients with low back and sciatic pain or motor or sensory loss of sciatic distribution.

J. V. Crawford

DISSEMINATED SCLEROSIS

1377. **The Serum Proteins in Disseminated Sclerosis.** (Das Serumweißbild bei der Multiplen Sklerose) E. NEUMAYER, F. PERGER, H. SCHINKO, and H. TSCHABITSCHER. *Wiener Zeitschrift für Nervenheilkunde* [Wien. Z. Nervenheilk.] 13, 46–64, 1956. 8 figs., 18 refs.

By means of paper electrophoresis 900 specimens of serum from 280 patients with disseminated sclerosis attending the University Neurological Clinic, Vienna, were examined, 430 samples of serum from 120 patients with other neurological disorders and 100 from normal subjects serving as controls. Of the patients with disseminated sclerosis, 36 had had the disease for periods up to 5 years, 64 for periods from 5 to 34 years and were showing steady progression without complications, and 180 had had the disease from 2½ to 22 years; in this last group complications such as bedsores and chronic urinary infection had arisen.

Only small differences in the different protein fractions were demonstrated, and these were subjected to statistical analysis. The main demonstrable difference was a diminished serum albumin and increased globulin level, particularly the γ -globulin fraction and less consistently the other globulin fractions. The longer the duration of the disease, the greater the increase in the serum γ -

globulin content. When the examinations were carried out at long intervals there was a change in the protein pattern corresponding to the state of the disease; thus a fall in the serum α -globulin level and a rise in the γ -globulin level usually indicated that a remission was imminent. (These changes are not specific for disseminated sclerosis and may be found in other chronic inflammatory processes.) The authors consider that the failure of other workers to demonstrate the changes here described can be attributed to the fact that the sera were not examined in relation to the stage or duration of the disease, and also that too few cases were studied.

G. S. Crockett

1378. **Isoniazid in Treatment of Multiple Sclerosis. Report on Veterans Administration Cooperative Study** VETERANS ADMINISTRATION MULTIPLE SCLEROSIS STUDY GROUP. *Journal of the American Medical Association* [J. Amer. med. Ass.] 163, 168–172, Jan. 19, 1957. 7 refs.

A cooperative clinical trial, conducted by 11 Veterans Administration hospitals according to a rigid protocol featuring randomization of therapy and control of observational error by means of a placebo and double-blind procedures, studied 186 patients (98 receiving a placebo and 88 isoniazid) with multiple [disseminated] sclerosis over a period of sufficient length to provide 122 patients with 9 months or more of follow-up. The patients represent nearly the entire spectrum of the disease as it is seen in males, with an adequate representation of those with recent activity. Detailed analysis of the observations, including subdivision of the series on the basis of 9 control variables, provides only a mass of negative data. It is believed that this investigation covers a sufficiently large number of patients in various stages of the disease, observed for an adequately long period, to conclude that isoniazid has no beneficial effect on the course of multiple sclerosis.—[Authors' summary.]

1379. **Treatment of Multiple Sclerosis with Low-fat Diet: Result of Seven Years' Experience**

R. L. SWANK. *Annals of Internal Medicine* [Ann. intern. Med.] 45, 812–824, Nov., 1956. 3 figs., 14 refs.

The author reports further observations made at the Montreal Neurological Institute on 153 patients with disseminated sclerosis who were given a low-fat diet, in some instances for as long as 6½ years, the daily fat content of the diet during the last 3½ years being 15 g. of animal or hard fat and 15 g. of vegetable or fish oil. The diet appeared to reduce the incidence and severity of exacerbations, especially in early cases. Performance improved or remained stable in 98 of the 153 patients (54 out of 59 early cases, 24 out of 36 intermediate cases, and 20 out of 58 late cases). Of the remaining 55, deterioration occurred in 5 early cases, 12 intermediate cases, and 38 late cases. The author recognizes that in the natural course of this disease, which has an average duration of 20 to 25 years, patients remain relatively well in the early stages and later deteriorate. It is hoped that continued follow-up of these patients will permit a definitive evaluation of these observations.

I. Ansell

Psychiatry

1380. **The Use of Glutamic Acid in Children with Down's Disease (Mongolism) and the Associated Changes in the Urinary Excretion of Certain Amino-acids.** (Применение глютаминовой кислоты и особенности выделения некоторых аминокислот у детей с болезнью Дауна) T. N. VOLKOVA and V. RUSSKIKH. *Журнал Невропатологии и Психиатрии* [Zh. Nevropat. Psikhiat.] 56, 750-756, 1956. 4 figs., 15 refs.

At the Paediatric Institute (Academy of Medical Sciences), Moscow, 33 children with Down's disease (mongolism) were treated with glutamic acid. Improvement in motor function, muscular tone, and mental alertness was found to occur most often in the younger patients, whereas in those aged 10 to 12 the treatment was often without effect. It is stressed that adequate duration of treatment (not less than 6 weeks) and optimum dosage are important for satisfactory results.

In addition to clinical criteria, the urinary excretion of tyrosine and of arginine were used as indices of the action of glutamic acid. The mean urinary concentration of tyrosine in the defective children was 25 to 30 mg. or more per 100 ml. (normal control values 10 to 12 mg. per 100 ml.) and of arginine 10 mg. or more per 100 ml. (normal 3 to 5 mg.). Glutamic acid was given orally in doses varying from 0.5 to 2 g. per kg. body weight per day. The excretion of tyrosine and of arginine diminished in parallel, reaching normal values when the dose of glutamic acid was approximately 1 g. per kg. per day. Increasing the dose above 1.5 g. per kg. resulted in a progressive and persistent rise in the excretion of both amino-acids. Intercurrent infections caused a temporary increase in the excretion of tyrosine, less so of arginine. The clinical improvement was in proportion to the reduction of excretion of the amino-acids; administration of excessive doses of glutamic acid resulted in the appearance of irritability, occasionally aggressiveness, and insomnia, but these signs quickly regressed on reducing or discontinuing the treatment. Observations were continued throughout a period of 3 months in each case.

The authors postulate that this type of mental deficiency is not, in its early stages, due to a degenerative process but rather to disorder of the anatomo-physiological development of the brain probably resulting from some endocrine imbalance. *Alexander Duddington*

1381. **Promedol Addiction.** (Привыкание к промедолу) M. A. GOL'DENBERG and M. S. SHAFRANOVA. *Советская Медицина* [Sovetsk. Med.] 75-77, No. 11, Nov., 1956.

Contrary to widely held opinion addiction to "promedol" [a drug closely resembling pethidine] can take place, and in this paper 9 cases are described. In many ways the condition resembles morphinism. Of the 9 patients investigated, 4 took the drug by sub-

cutaneous injection, one orally, and 4 by intravenous injection (which is not a method recommended in any literature on the subject available to the authors). The largest amount of the drug taken intravenously by these patients was 200 ml. of a 2% solution (that is, 25 times the therapeutic dose), while the largest daily dose taken subcutaneously was 40 ml. of a 2% solution (10 times the therapeutic dose); the maximum daily oral dose was 0.25 g. Some of the patients took promedol only when morphine was not available, sometimes resorting to one drug, sometimes to the other. Several of them had been taking promedol for 1½ to 2 years.

Withdrawal symptoms were somewhat less severe and of shorter duration than in morphine addicts. In view of the widespread use of promedol in surgery, medicine, and obstetrics the authors urge that this drug should be administered in such a way as to avoid the danger of causing addiction. *L. Firman-Edwards*

1382. **Use of Reserpine ("Serpasil") in the Management of Chronic Alcoholism**

R. E. WELLS. *Journal of the American Medical Association* [J. Amer. med. Ass.] 163, 426-429, Feb. 9, 1957. 5 refs.

A study was made of 145 ambulatory patients undergoing treatment [at the Peter Bent Brigham Hospital, Boston] for chronic alcoholism. A double-blind study with reserpine ("serpasil") and a placebo revealed that approximately half the patients treated in an out-patient clinic were significantly improved on reserpine therapy. One-fourth were slightly improved and one-fourth were unchanged. Of the 33 patients receiving placebo therapy under the same conditions, 29 (87%) showed no significant improvement.—[Author's summary.]

TREATMENT

1383. **Effects of Chlorpromazine on Chronic Lobotomized Schizophrenic Patients. A Controlled Study**

H. FREEMAN and H. S. CLINE. *A.M.A. Archives of Neurology and Psychiatry* [A.M.A. Arch. Neurol. Psychiat.] 76, 500-507, Nov., 1956. 2 figs., 5 refs.

At Worcester (Massachusetts) State Hospital 20 chronically disturbed male schizophrenic patients who had previously undergone lobotomy were divided into two equal groups matched in respect of results on a modified Malamud-Sands Rating Scale (15 items assessing the degree of deviation from normal) and of age, duration of stay in hospital, and years since lobotomy. Group 1 was given a placebo, while Group 2 received chlorpromazine, 200 mg. daily for the first 4 weeks, 400 and then 600 mg. daily for successive periods of 2 weeks each, 800 mg. daily for the next 3 weeks, and finally a placebo for the last 4 weeks. The study was conducted in such a way that neither the rating psychiatrist nor

the ward personnel knew the nature of the medication any particular patient was receiving.

The mean rating scores for patients in Group 2 showed a sudden fall (indicating improvement) in the first week of treatment, followed by fluctuation but no consistent change during the subsequent 7 weeks. When the dosage of chlorpromazine reached 800 mg. daily, however, the mean score showed a further decrease within one week and continued to fall irregularly during the next 2 weeks, suggesting that for this group the threshold dosage lay between 600 and 800 mg. daily. When chlorpromazine was replaced by the placebo in the treatment of Group 2 there was no essential change in the mean score for the first 3 weeks, but in the fourth week the score rose again and reached a level higher than that preceding the period of treatment with 800 mg. daily. Thus in general the level of scores for the two groups was essentially the same for the first 8 weeks, but when the dosage of chlorpromazine reached 800 mg. daily the values for the two groups began to show clear differentiation.

Trends were analysed by summing for each subject in both groups the scores obtained during two contrasted periods, namely, the 3 weeks before Group 2 received 800 mg. of the chlorpromazine daily and the 3 weeks during which this dosage was given. During the first period the difference was not statistically significant, but during the second it was markedly so. Similar comparisons were made for individual items on the rating scale. For Group 1 none of the differences was significant, but for Group 2 eight items showed significant trends from their base-line value in the direction of improvement; however, if the variations in Group 1 were considered, only four items were significantly improved in Group 2, namely, responsivity, socialization, perception, and thought processes. As stated, when the drug was discontinued there was reversion to the previous score, and analysis of individual items suggested that the drug had had a merely suppressive effect.

No serious side-effects were observed, and such signs and symptoms as unsteadiness and mask-like facies disappeared on withdrawal of the drug. There was no correlation between the threshold dosage of chlorpromazine and age, duration of the illness, years since lobotomy, or clinical status as evidenced by rating score.

John C. Kenna

1384. Preliminary Observations on Use of Frenquel in Hospital Psychiatry

S. COHEN and R. R. PARLOUR. *Journal of the American Medical Association [J. Amer. med. Ass.]* 162, 948-950, Nov. 3, 1956. 8 refs.

The authors, from the Neuropsychiatric Hospital, Veterans Administration Center, Los Angeles, report the results obtained with "frenquel" (α -(4-piperidyl)-benzhydrol hydrochloride) in the treatment of 100 psychotic patients. The usual dosage was 100 mg. initially by intravenous injection followed by 80 to 180 mg. daily by mouth. A few patients were subsequently given 1,200 mg. daily for 3 weeks, but there was no further improvement with this regimen although no toxic effects were observed.

Of 11 patients suffering from acute disturbances of behaviour, whether schizophrenic, manic, or delirious in origin, 8 showed a definite response to frenquel. In less disturbed patients there was relatively little improvement, and of 30 quiet chronic patients, 24 showed no change, while in 6 the response was "slight or questionable". Anxiety in non-psychotic patients was unaffected. There was no evidence that frenquel had any antihallucinatory action.

Many of the patients had previously received reserpine and chlorpromazine. In general, the beneficial effect of frenquel was comparable to that of the other two drugs; however, frenquel did not result in the sedation and loss of spontaneity that are sometimes seen with reserpine and chlorpromazine. In a few instances frenquel combined with reserpine or chlorpromazine produced a response which was not achieved with one drug alone.

L. G. Kiloh

1385. Therapeutic Process in Electroshock and the Newer Drug Therapies. Psychopathological Considerations

L. ALEXANDER. *Journal of the American Medical Association [J. Amer. med. Ass.]* 162, 966-969, Nov. 3, 1956. 3 figs., 15 refs.

In this discussion, from Boston State Hospital, of the nature of the therapeutic process in electric convulsion therapy (E.C.T.) the author states that depression is not a defence against anxiety but a state of overwhelming anxiety with hopelessness. By the use of E.C.T., it is claimed, depression can be changed into anxiety and the reconversion can be achieved by non-convulsive electrostimulation.

The primary, underlying, traumatic neurosis is not relieved by E.C.T., but the secondary or warning anxiety, characterized by either panic or depression, is relieved. The warning anxiety is stated to be subcortical and largely unconscious, whereas the depression or panic is cortical and conscious. E.C.T. is thought to operate by reducing cortical excitability so that the warning anxiety can no longer overstimulate the "cortical ego" into panic or depression. In cases of severe depression the author prefers to "ventilate" the warning anxiety by the additional use of non-convulsive stimulation, E.C.T. being used only to "pave the way for subsequent psychotherapy of the primary traumatic conflict". The tranquillizing drugs are thought to suppress cortical anxiety, and an elaborate explanation is given as to why they should have a "superb effect" in manic states. [Unfortunately this argument demands that manic states should not respond to E.C.T.—which is hardly the general experience.] On the other hand these drugs aggravate depression or leave it unaffected, because the ego has already been inhibited or paralysed by the illness. The action of other new substances, such as meprobamate and benactyzine, which are described as relaxant or "antiphobic" drugs, is referred to briefly.

[Several "parlour game" diagrams which match the terminology are reproduced. The article is largely an attempt to explain the efficacy of E.C.T. in the treatment of depression.]

L. G. Kiloh

Dermatology

1386. Psoriasis and Arthritis

V. WRIGHT. *British Journal of Dermatology* [Brit. J. Derm.] 69, 1-10, Jan., 1957. 4 figs., 36 refs.

The relationship between arthritis and psoriasis was studied by analysing 3 groups of patients at Stoke Mandeville Hospital, Bucks: (1) 42 with psoriasis and arthritis, of whom 34 had "erosive arthritis" (a term which the author uses in preference to "rheumatoid arthritis" in order not to prejudge the issue), 6 with degenerative joint disease, one with rheumatic fever, and one with gout; (2) 55 with rheumatoid arthritis, unselected except that in all cases the Waaler-Rose differential agglutination test (D.A.T.) gave a positive response; and (3) 310 unselected patients suffering from psoriasis only.

Of the 34 patients with psoriasis and "erosive arthritis", 94% gave a negative D.A.T. response, and this suggests that the joint condition in these cases forms an entity distinct from rheumatoid arthritis. A less likely explanation is that the psoriasis modifies the arthritis. Clinical differences from the classic picture of rheumatoid arthritis in Group 1 included a high incidence of distal interphalangeal joint involvement (58%), a combination of ankylosing spondylitis and peripheral arthritis in 3 cases, and a generally milder course than in Group 2. Nail changes characteristic of psoriasis were seen in 87% of Group 1 as against 18% of Group 3. The psoriasis seen in Group 1 differed in some respects from that in similar cases reported in the literature in that it was not extensive, never pustular, not unduly resistant to treatment, and did not usually affect the palms and soles.

[This is a notable contribution to a controversial subject.] G. W. Csonka

[Another paper dealing with the same series of cases primarily from the rheumatological aspect was published in *Annals of the Rheumatic Diseases* for December, 1956. See Abstract 1344.—EDITOR.]

1387. Pemphigus Neonatorum. (Пузырчатка новорожденных (Материалы к клинике этиологии, патогенезу и эпидемиологии))

L. I. GOKINAeva. *Вестник Венерологии и Дерматологии* [Vestn. Vener. Derm.] 14-18, No. 6, Nov.-Dec., 1956 [received Feb., 1957]. 2 figs.

A series of 6 different outbreaks of pemphigus neonatorum involving 22 infants was studied at the Pavlov Medical Institute, Leningrad. Fluid was obtained by the puncture of fresh bullae and 292 cultures were made on different media including blood agar. In 282 cases a pure growth of *Staphylococcus aureus* was obtained, in 4 cases a growth of *Pseudomonas aeruginosa*, and in 8 cases the culture was sterile. In no case could the author obtain a growth of streptococci even in the most favourable conditions.

Intradermal testing with sterile staphylococcal toxin gave positive reactions in all the sick babies and negative reactions in healthy infants. Hyperhidrosis was a marked feature in all cases, but the pH of the skin was not changed. The source of infection in each outbreak was traced to the nursing staff or to the mothers of infected infants.

H. Makowska

1388. The Mother-Child Relationship in the Genesis of Neurodermatitis

J. MARMOR, M. ASHLEY, N. TABACHNICK, M. STORKAN, and F. McDONALD. *A.M.A. Archives of Dermatology* [A.M.A. Arch. Derm.] 74, 599-605, Dec., 1956. 17 refs.

In recent years a number of workers have stressed the importance of the nature of the early relationship with the mother in the genesis of "neurodermatitis" in children. The most common finding has been maternal rejection. This study, reported from the County General Hospital, Los Angeles, is a further exploration of this aspect of the subject. The mothers of 22 children with neurodermatitis were interviewed. It appeared that the child had been rejected, neglected, or separated from its mother in every case. Rejection (13 cases) was manifested in neglect, failure to pick up and caress the child, or less often in rough handling. Psychological tests were given to the 10 mothers who were willing to cooperate. All of them were shown to be of considerable emotional immaturity, with feelings of frustration, and many were consciously or unconsciously hostile to their husbands. There was no overt anxiety, but inner tensions were present. Thus the importance of a disturbance in the mother-child relationship was confirmed.

Maternal rejection, however, was by no means invariable. In about one-third of the cases the separation of the child from the mother was due to circumstances unconnected with emotional factors, poverty and the necessity for the mother to go out to work often playing an important part; in half the cases there was overt marital friction in the family. In discussion the authors point out that on the other hand most infants who are neglected or rejected do not suffer from neurodermatitis, and the hereditary factor is probably therefore of great importance in this condition; in 19 of the 22 patients (86%) there was a family history of skin disorder. It has been suggested that neurodermatitis is one of the "disorders of adaptation" in the reaction to stress. Any personality types which may be attributed to sufferers from neurodermatitis are probably the result rather than the cause of the condition. Thus individuals with chronic disfiguring diseases of the skin are likely to be sensitive about their appearance and to seem much concerned with themselves and may therefore easily be dubbed "narcissistic". It is concluded that hereditary, psychological, physiological, and sociological factors are all concerned in the causation of this disease.

E. Lipman Cohen

Paediatrics

1389. The Complete Elimination of Retrolental Fibroplasia

P. BANISTER and J. C. LOCKE. *Canadian Medical Association Journal* [Canad. med. Ass. J.] 76, 81-85, Jan. 15, 1957. 4 figs., 8 refs.

It is pointed out that in spite of advances in measures for the prevention of retrolental fibroplasia cases of this condition still occur. A considerable reduction in the incidence of the disease was achieved before July, 1954, by reducing the amount of oxygen given to premature infants to minimal safe levels; nevertheless 6 out of a series of 118 infants weighing less than 4 lb. (1.8 kg.) at birth developed the condition. At the Royal Victoria and the Catherine Booth Mothers' Hospitals, Montreal, further safety measures have been adopted since July, 1954, and of 126 infants weighing less than 4 lb. at birth, none showed any evidence at any stage of retrolental fibroplasia.

Oxygen was not curtailed during resuscitation, but after transfer of the infant to the incubator oxygen was given only in the presence of cyanosis due to arterial blood desaturation, respiratory distress, poor colour and reduced activity after oxygen cessation, and pallor after feeding. The concentration of oxygen permitted never exceeded 40%, unless this proved ineffective; this was a rare occurrence. The degree of arterial oxygen saturation was always estimated in these infants. Generally, oxygen levels were recorded every 2 hours with a Beckmann Model D oxygen analyzer, these determinations being made more frequently when adjustments were made to the incubator. Of the total of 126 infants, 32 received no oxygen and a further 44 needed it for only 24 hours.

The authors consider that by their methods retrolental fibroplasia has been prevented. They recommend that the measuring and recording of oxygen concentrations should be charted in the same way that doses of potentially toxic and lethal drugs are charted, and that the nursing staff should be trained for the responsibility of decreasing or increasing oxygen concentration as necessary. Finally, the eyes of the infant should be examined before it is discharged, so that if there are signs of the disease the methods of administration of oxygen in general can be investigated. J. G. Jamieson

1390. Spontaneous Pneumothorax in the First Ten Days of Life

V. M. HOWIE and A. S. WEED. *Journal of Pediatrics* [J. Pediat.] 50, 6-15, Jan., 1957. 40 refs.

Pneumothorax in the newborn has been described from time to time during the last 80 years, and in some periods and at certain clinics it has been regarded as a frequent finding (up to 37.5%). The present authors suggest that failure to recognize artefacts and misreading of x-ray films of unsatisfactory quality has

artificially increased the figures in such cases. They define the condition as the presence of gas in the pleural space, demonstrated by x rays or post mortem, without obvious cause such as infection or surgery. The following varieties have been described: mantle pneumothorax (a small partial pneumothorax, the lateral border of the lung being shown parallel to the thoracic wall), alternating, bilateral, and tension. Of these, the important type is tension pneumothorax, the presence of which is suggested in the radiograph by a contralateral mediastinal shift with widening of the homolateral intercostal spaces and depression of the homolateral diaphragm. The diagnosis is proved by finding gas under pressure on thoracocentesis.

The authors summarize the previously reported cases of alternating, bilateral, and tension pneumothorax arising in babies of 10 days and under and add 9 cases of their own from the Los Angeles Children's Hospital and a U.S. Air Force hospital. They consider the incidence to be of the order of 0.07% as estimated by Harris and Steinberg in a series of 8,716 newborn babies. They accept the aetiological theory of pulmonary interstitial emphysema leading to mediastinal emphysema and so to pneumothorax. No treatment is needed except for cases of increasing or tension pneumothorax, and here they regard continuous drainage with an under-water trap as life-saving. This treatment has, of course, no effect on the pulmonary or mediastinal emphysema, or on any accompanying hyaline-membrane formation or pneumonia. A. White Franklin

1391. Congenital Toxoplasmosis Simulating Haemolytic Disease of the Newborn

A. D. BAIN, J. H. BOWIE, W. F. FLINT, J. K. A. BEVERLEY, and C. P. BEATTIE. *Journal of Obstetrics and Gynaecology of the British Empire* [J. Obstet. Gynaec. Brit. Emp.] 63, 826-832, Dec., 1956. 8 figs., 35 refs.

Attention is drawn to the difficulty of differentiating haemolytic disease of the newborn from toxoplasmosis, and 3 cases of congenital toxoplasmosis are described. In the first infant, who was stillborn and severely hydropic, the placenta was large and fleshy as in haemolytic disease. Serological examination of both mother and infant confirmed the diagnosis of active toxoplasmosis, and *Toxoplasma* was isolated from the infant by means of animal inoculation. The second infant died immediately after birth, the gestation period having been 35½ weeks. The placenta was large and flabby, and in this case also the diagnosis of toxoplasmosis was established on serological examination of mother and infant and *Toxoplasma* was isolated. In the third case, that of a stillborn macerated foetus of 30 weeks' gestation, no serological findings on the infant were available and attempts to isolate the organism were unsuccessful, but 2 days after the birth the mother's reaction to the dye

test was positive at 1:10,000 and to the complement-fixation test at 1:64. All 3 infants had enlarged spleens and 2 had enlarged livers. Haemolytic disease of the newborn was excluded in all cases by the haematological findings.

Some of the problems of diagnosis are discussed, and attention is drawn to the length of time which may be necessary for the isolation of *Toxoplasma* in laboratory animals.

I. A. B. Cathie

1392. The Effect of Maternal Anoxaemia on the Foetal Haemoglobin of the Newborn

Y. M. BROMBER, A. ABRAHAMOV, and M. SALZBERGER. *Journal of Obstetrics and Gynaecology of the British Empire* [J. Obstet. Gynaec. Brit. Emp.] 63, 875-877, Dec., 1956. 1 fig., 11 refs.

The object of an investigation reported from Hadassah University Hospital, Jerusalem, was to determine whether a reduced oxygen supply to the foetus, due to conditions in the mother, would lead to an alteration in the foetal-haemoglobin concentration in the blood of the foetus. In 100 healthy infants the foetal-haemoglobin value varied from 61 to 95%, with an average of 86.5%. In 12 newborn infants suffering from asphyxia due to such conditions as premature separation of the placenta, mishaps to the cord, and prolonged labour, the foetal-haemoglobin concentration was normal. In 10 out of 12 infants newly born to mothers suffering from chronic anoxaemic conditions in pregnancy, abnormally high foetal-haemoglobin values ranging from 94.5 to 100% were found. The authors assume that this high foetal-haemoglobin concentration is due to adaptation on the part of the foetus, and it is noted that follow-up in these infants showed normal replacement of the foetal haemoglobin by the adult type.

I. A. B. Cathie

1393. Listeriosis of the Newborn. (La listériose du nouveau-né)

G. COULOMBIER, S. SARRUT, F. ALISON, and A. ROSSIER. *Archives françaises de pédiatrie* [Arch. franç. Pédiat.] 13, 943-960, 1956. 4 figs., bibliography.

From the Hôpital St. Vincent-de-Paul and the School of Paediatrics, Paris, the authors report 2 cases of infection with *Listeria monocytogenes* in newborn babies. The organism was first isolated by Hulpers in 1911 from rabbit's blood. Like toxoplasmosis, listeriosis is largely an infection of animals, but may cause a mild illness in pregnant women with severe congenital infection of the foetus. The organism is a Gram-positive, round-ended bacillus surviving storage for long periods at laboratory temperature or in the cold. It is motile, likes glucose, and grows rapidly on routine culture media. Mice are susceptible and develop small necrotic lesions in the liver. There are four serological types. Agglutinins and deviation of complement occur in affected mothers. The histological lesion resembles that of miliary tuberculosis, the milia being composed of islets of cell necrosis up to 0.5 mm. in diameter, with no leucocytic infiltration, but with a few organisms present at the periphery which can be readily cultured. The clinical picture is varied,

with two main types, meningitic and septicaemic. In both there are fever, drowsiness or excitement, vomiting, and an appearance of extreme illness. In the meningitic type in the newborn the baby is "cerebral", with cyanotic attacks, disturbed respiratory rhythm, and sometimes fits. The cerebrospinal fluid is cloudy, with 40 to 75 mononuclear cells per c.mm. In 5 of the 11 recorded cases of this type the patient has survived after treatment with sulphonamides or antibiotic drugs. The septicaemic type usually affects premature babies and is generally fatal after a few hours or days. Severe jaundice with purpura was present in one of the authors' 2 cases of which full details are given; both were fatal.

Listeriosis is found in many species scattered over the globe. Morbidity is rarely more than 10%, but among the affected animals the mortality is high. The reservoir is unknown. In experiments on rabbits the organism has been found in the foetus after the oral or ocular infection of the pregnant female, whereas males and non-pregnant females had only a short, localized illness. In human cases the mother may have had a short febrile illness a few days or weeks before delivery, the nature of which may be established by means of the complement-fixation test. The authors suggest that maternal infection, whether or not it gives rise to clinical illness, leads to transplacental infection of the foetus and infection of the liquor through the foetal urine, followed by abortion or premature birth of an infant with septicaemia.

Infection in the labour ward following the delivery of infected mothers has been reported, and the infection can be acquired later in infancy. Treatment with sulphonamides and penicillin in combination is effective. The organism is also sensitive to aureomycin, oxytetracycline, and erythromycin, but resistant to chloramphenicol, streptomycin, and polymyxin. Prophylactic chemotherapy in cases of infection of the pregnant woman has been described as leading to the birth of a normal, unaffected baby.

A. White Franklin

CLINICAL PAEDIATRICS

1394. Chronic Staphylococcal Enteritis in Infants

J. U. CRICHTON. *Journal of Pediatrics* [J. Pediat.] 49, 553-557, Nov., 1956. 6 refs.

A syndrome of enteritis in infants which appeared to be due to *Staphylococcus* is described, and 9 cases, the majority of which were seen at the General Hospital, Calgary, Alberta, are reported. Clinically, there was diarrhoea with foul-smelling stools containing mucus and sometimes blood. The infant was artificially fed, and became fussy rather than acutely ill. In some instances symptoms had been present since the neonatal stage. On stool culture *Staph. aureus* was the only known pathogen found. One of the infants died, and necropsy revealed massive growth of the organism in necrotic mucosa of the small intestine. Antibiotics, including erythromycin, chloramphenicol, streptomycin, and penicillin, were administered as indicated by disk sensitivity tests. These were much more effective when given systemically than when given by mouth to act on

the intestine. Early diagnosis appeared to improve the prognosis, successful treatment becoming more difficult after the lapse of time. In a discussion it is stated that since there were clinical grounds for suspecting that infection occurred in the hospital nursery, stool samples from all infants discharged over a period of one week were cultured. Coagulase-positive staphylococci were found in the stools of 10 of 43 such infants; none of these, 7 of whom were breast-fed, developed any symptoms of enteritis up to 6 weeks, and they could therefore be considered to be carriers.

The author comments on the absence of references to this condition in the literature and concludes that there has been a recent increase in incidence and in awareness of the different manifestations of staphylococcal infection. He emphasizes that the condition appears to be on the increase, at least in the region of the Calgary General Hospital, and that it may be mild in form, simulating a disturbance of feeding. Nevertheless it can be the cause of chronic ill health. It is recommended that in all cases of diarrhoea in the first few weeks of life stool specimens should be cultured for the presence of staphylococci.

E. H. Johnson

1395. Developmental Speech Anomalies in Apparently Normal Children

C. H. M. WALKER and P. R. LANGUTH. *British Medical Journal* [Brit. med. J.] 2, 1455-1458, Dec. 22, 1956. 18 refs.

In an attempt to determine the cause of speech anomalies in apparently normal children the authors have investigated the very early development of 52 children who attended the Speech Clinic of the Hospital for Sick Children, Great Ormond Street, London, for the treatment of delayed onset of speech, arrested speech development, and subsequent dyslalia. These children had no physical abnormalities and were of average intelligence, none having an I.Q. below 80. These 52 cases represented about 8% of the work of the clinic. The ratio of boys to girls was 2 to 1, but no particular defect was selective for either sex.

It was found that arrested speech development was much more frequent than delayed onset of speech, which occurred in only 7 cases. The babbling of infants is taken to constitute the beginning of speech. When the correct formation and use of words was delayed beyond the age of 2 years an abnormality was considered to be present. In all but 5 cases the late use of words was accompanied or followed by dyslalia which was most often multiple, the most general difficulty being in the formation of consonants. Other defects were "cluttering", idioglossia, monosyllabism, echolalia, rhinolalia, sigmatism, multiple d-substitution, rejection of speech, and hysterical mutism. It is suggested that the causes of speech defects appear to be largely psychological. Bad family relationships, the birth of another child, separation from home, lack of stimulation, overprotection, and other factors all played some part. In 7 cases the patient was the youngest of a large family. Among the older children there were 9 cases of nocturnal enuresis. Apart from environmental factors it is thought

that genetic influences may also be involved. These would to some extent explain the greater incidence in boys, and the fact that in this series similar difficulties of speech had occurred in other members of the families of about one-third of the patients. [This fact could equally be taken as evidence of the effect of environmental factors.]

Tests for crossed laterality showed that this was unlikely to play an important part, the incidence being 26%, which is very close to the incidence in the normal school population. There was only one case of complete left laterality. In 12 (37.5%) of the 32 children already of school age progress at school was impeded by the speech defect. It is recommended that treatment should be begun between the ages of 3 and 4; there is then a good chance that the defect may be remedied before the child starts school. Treatment should be on general lines at first, and attendance at a nursery school may be all that is necessary. Where possible, psychological causal factors should of course be removed. A few of the severe cases may perhaps be due to delayed specific neurological development, and these cases will not be helped by speech therapy.

Marianna Clark

1396. Quantitative Assessment of Motor Function in Cerebral Palsy. Evaluation of Zoxazolamine (Flexin), a New Muscular Relaxant Drug

J. G. MILLICHAPE and R. HADRA. *Neurology* [Neurology] 6, 843-852, Dec., 1956. 4 figs., 11 refs.

Simple quantitative tests devised by the authors at the National Institute of Neurological Diseases and Blindness, Bethesda, Maryland, for the assessment of motor function in children with cerebral palsy are described. They included estimation of the range, speed, power, and coordination of voluntary movements, and kymographic and other tests of balance. A technique is also described which makes it possible to assess the extent to which improvement in performance is due to practice.

These tests were used to evaluate the treatment of 10 children with cerebral palsy with zoxazolamine ("flexin", 2-amino-5-chlorobenzoxazole). Four of the children had spastic quadriplegia, 2 spastic hemiplegia, and 4 athetosis. The drug was given in doses of 0.75 to 1.5 g. daily for periods of a month, alternating with placebo tablets for similar control periods. The drug depresses polysynaptic pathways in the spinal cord, having a more prolonged action than mephenesin and only a weak neuromuscular blocking action. Significant improvement occurred in 6 cases, being most evident in cases of athetosis without weakness. Side-effects such as nausea, vomiting, urticaria, and an increase in the frequency of fits occurred in 4 cases. In a limited comparative trial chlorpromazine (one case) and reserpine (4 cases) tended to impair functional ability, although the former has been shown to diminish spasticity.

J. Foley

1397. Jaundice in Childhood

F. ARDEN. *Medical Journal of Australia* [Med. J. Aust.] 1, 316-318, March 9, 1957. 1 ref.

Public Health and Industrial Medicine

1398. A Contribution to the Epidemiology of Q Fever. (Ein Beitrag zur Epidemiologie der Q-Rickettsiose.)

K. RAŠKA and L. SYRŮČEK. *Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene. I. Abt. Originale* [Zbl. Bakt., I. Abt. Orig.] 167, 267-280, Dec., 1956. 11 refs.

The authors report investigations into the epidemiology of Q fever in Czechoslovakia during the period 1952-6, when a number of outbreaks of varying size occurred among dairy farmers and meat workers. The examination of the patients' blood revealed a high antibody titre against *Rickettsia burneti*. The principal sources of human infection were cattle, sheep, and goats, but epizootic outbreaks occurred among various mammals and birds, as demonstrated by serological examination and the isolation of *R. burneti* from certain organs, faeces, urine, placenta, and foetal membranes. Human beings are infected either by inhaling dust which is contaminated with the excreta of animals or by drinking infected milk.

Amongst other anti-epidemic measures the authors recommend the notification of the disease in man and domestic animals, the investigation of the possible sources of infection by the serological examination of cattle, sheep, and goats, and improvement of the sanitary regulations governing imported animals and raw materials such as wool, cotton, and leather.

Franz Heimann

1399. The Varying Epidemiology of Q Fever in the South-East Region of Great Britain. I. In an Urban Area

B. P. MARMION and M. S. HARVEY. *Journal of Hygiene* [J. Hyg. (Lond.)] 54, 533-546, Dec., 1956. 2 figs., 15 refs.

After an outbreak of Q fever had occurred in a London hospital in 1949 the authors investigated the cases of 160 persons, inhabitants of two adjoining coastal towns in north-east Kent, who had had either pneumonia or undiagnosed fever during the period 1948-54. Only a short stretch of open country separates the two towns, whose populations are 18,228 and 17,200 respectively, and the coastal road divides them from the surrounding country on the landward side. The patient who originated the outbreak in the London hospital came from one of these towns, and *Rickettsia burneti* was isolated from his household milk supply. Of the persons examined, the blood of 22 contained complement-fixing antibody to *R. burneti* at titres of 1:40 or more, this level having been accepted as evidence of a clinical attack. Out of 240 healthy blood donors who were studied as controls, only in 2 did the blood contain a significant titre of antibody.

In 21 out of the 23 cases of Q fever (including the original case) the household consumed raw milk, com-

pared with 92 out of 137 control cases, while 22 of the 23 households received their milk supply from one or other of 5 out of the 16 dairies serving the town, 13 of these 22 patronizing one of 2 dairies. Samples of milk from 29 local herds were biologically tested for *R. burneti* during 1949-54 and the organism was demonstrated in 3 (10%) of these herds: these 3 herds supplied the 2 retail dairies which were associated with 13 cases of Q fever. A history of occupational or other regular contact with animals or their products was no more common in the Q-fever group than among the controls. There was no significant difference in sex distribution and no apparent seasonal trend.

The authors conclude that the Q fever in these two towns was predominantly milk-borne. J. Cauchi

1400. The Varying Epidemiology of Q Fever in the South-east Region of Great Britain. II. In Two Rural Areas

B. P. MARMION and M. G. P. STOKER. *Journal of Hygiene* [J. Hyg. (Lond.)] 54, 547-561, Dec., 1956. 1 fig., 10 refs.

An investigation into the occurrence of Q fever in man and animals was carried out in the Romney Marsh area (population 9,247) in Kent and in the Chatteris-North Witchford area (population 10,662) in Cambridgeshire. The two areas are similar geographically and meteorologically but the former is devoted mainly to sheep farming, whereas there are few sheep in the latter. Both areas have about the same number of cattle, but more pigs and probably more goats are kept in the Chatteris-Witchford area. The purpose of the investigation was to determine how far sheep were acting as a source of infection of human beings with Q fever in the former area.

In Romney Marsh the authors investigated the cases of 95 persons, including some children, with a history of pneumonia or unexplained fever during 1949-54: the blood of 13 of these was found to contain complement-fixing antibody to *Rickettsia burneti* at the significant titre of 1:40 or over. In Chatteris-Witchford none of the 50 persons who had had pneumonia or undiagnosed fever during the same period showed any evidence of a recent attack of Q fever. Healthy blood donors and adult volunteers were studied as controls.

Of the 13 cases of Q fever in Romney Marsh, 5 were in agricultural workers in contact with sheep, while 9 of the 13 patients began their illness during the lambing and shearing season (April-June). Three flocks of sheep were tested and their blood found to contain antibody to *R. burneti*, while a strain of *R. burneti* was isolated subsequently from the placenta and wool of sheep in one of these flocks. Two of the 5 agricultural workers affected drank raw milk; the bulked milk and the cattle belonging to the herd which supplied the

household of one of these 2 workers were tested and no evidence of infection found. However, bulked milk from 2 of the 17 dairy herds in Romney Marsh contained *R. burneti*. It is known that cattle tend to be more commonly infected in areas where there are numerous sheep. A substantial proportion of the inhabitants of the Chatteris-Witchford area consumed raw milk and were in contact with cattle. Milk from all the local dairy herds was biologically tested for *R. burneti* and found negative; 92 cows from 11 of the 16 herds in the area were serologically examined and showed no evidence of infection.

The authors conclude that sheep in the Romney Marsh area appear to act as one source of infection for man, though infection from raw milk may have been responsible for some of the cases.

In Romney Marsh previous investigations have established that the sheep tick, *Hæmaphysalis punctata*, is infected with *R. burneti*, though Q-fever infection was observed in a flock which was virtually tick-free. Organs from 229 rabbits and 30 other small animals were examined by guinea-pig inoculation with negative results: the organs of 166 wild birds of various species were also examined, but *R. burneti* was not isolated.

J. Cauchi

1401. Deaths from Poliomyelitis among British Doctors
R. DOLL and A. BRADFORD HILL. *British Medical Journal* [Brit. med. J.] 1, 372, Feb. 16, 1957. 1 ref.

Between November, 1951, and September, 1956, among 34,494 doctors practising in Great Britain 8 deaths from poliomyelitis were recorded. The authors point out that while 8 is a very small number, only one would have been expected to occur if doctors were dying from this disease at the same rate as adult males in the general population. Doctors aged 25 to 45 appear to be at special risk of contracting poliomyelitis or, having contracted the disease, of dying from it.

Derek R. Wood

1402. Vaccination with Avianized Smallpox Vaccine
M. WEICHSEL and E. G. HERRERA. *Journal of Pediatrics* [J. Pediat.] 50, 1-5, Jan., 1957. 1 fig., 13 refs.

Comparative investigations of three different types of vaccinia vaccine were carried out at Sea View Hospital, Staten Island, New York, on 414 children whose ages varied from 3 months to 12 years. The children were divided into three groups, 285 being vaccinated with glycerinated chick-embryo vaccine, 44 with fluid sorbitol-stabilized chick-embryo vaccine, and 85 with vacuum-dried sorbitol-stabilized chick-embryo vaccine. The results with each type were satisfactory, 358 out of 371 children with no history of previous vaccination showing a typical primary reaction. Of the 43 who had a history of previous vaccination, all of whom received the vacuum-dried vaccine, 22 gave an accelerated reaction and 21 an immune reaction. Side-reactions were mild and no complications were observed. The advantage of the vaccinia virus prepared on the chorio-allantois of the developing chick embryo over calf-lymph virus vaccine lies in its production in larger quantities within a shorter period.

Franz Heimann

1403. Changing Patterns in the Causes of Death at the Hospital for Sick Children

C. O. CARTER. *Great Ormond Street Journal* [Gt Ormond Str. J.] No. 11, 65-68, 1956. 1 fig.

A comparative analysis is presented of the cause of death (confirmed at necropsy), in the first 200 children dying at Great Ormond Street Hospital in each of the years 1914, 1934, and 1954-5. For the purposes of the investigation four disease groups based on aetiology are recognized: (1) environmental diseases; (2) diseases of unknown origin; (3) diseases partly genetic; and (4) diseases accepted as wholly genetic. In 1914 environmental diseases, chiefly tuberculosis, pneumonia, and gastroenteritis, caused 68% of the deaths, diseases of unknown origin 15½%, diseases partly genetic 14½%, and diseases wholly genetic 2%. By 1954 the death rate from environmental diseases had fallen to 14½%, the figures for the other groups being 48%, 25½%, and 12% respectively (in 1954 Group 4 included 18 cases of fibrocystic disease of the pancreas). The figures for 1934 occupy an approximately intermediate position.

The author considers that in the future there will be a further reduction in mortality from diseases in Group 1 and that mortality in Group 2 will be affected by a reallocation of many cases "perhaps the majority going to Group 3". With regard to genetic predispositions, he states that a reduction in the number of children born with genetic predisposition to disease depends essentially on reducing the survival time, in terms of generations, of the gene mutations responsible.

R. J. Matthews

INDUSTRIAL MEDICINE

1404. The Effects of the Temperatures of the Floor Surface and of the Air on Thermal Sensations and the Skin Temperature of the Feet

F. A. CHRENKO. *British Journal of Industrial Medicine*, [Brit. J. industr. Med.] 14, 13-21, Jan., 1957. 4 figs., 21 refs.

It is self-evident that serious discomfort may ensue if floor heating is excessive, although the risk of discomfort probably varies with the posture and activity of the occupants of the room. Estimates of the surface temperature above which discomfort is liable to occur range between 75° and 85° F. (23.9° and 29.4° C.).

At the Medical Research Council Laboratories, London, experiments were performed on 5 men and 3 women in order to assess the effect of heated floors upon the temperature of the feet. Wearing normal shoes and clothing, the subjects either walked for one hour or sat with their feet on a heated floor. Changes in the surface temperature were obtained by varying the power supplied to electrical resistance mats attached to the underside of the floor-boards. The temperature of the air ranged from 58° to 76° F. (14.4° to 24.4° C.). Draughts were avoided by keeping the doors and windows closed, and the effects of solar radiation were reduced by means of large window screens of aluminium foil.

Thermal sensations were assessed by the subjects on an arbitrary numerical scale and the skin temperature was

measured at the beginning, middle, and end of each period of exposure. Probit analysis of the subjects' responses showed that similar degrees of discomfort were produced in both men and women at a lower floor temperature when the subject was walking than when sitting and that tolerance of a warm floor was more closely related to activity than to the nature of the footwear. The highest temperature at which no discomfort was reported while walking was 77° F. (25° C.). Discomfort was related to an increase of skin temperature, especially on the soles, the temperature at which the incidence of discomfort began to rise rapidly being about the same as that at which a rapid increase in blood flow might be expected. With reduced air temperatures higher floor temperatures could be tolerated. Measurements with mercury-in-rubber strain gauges failed to show any significant change in girth of the instep and ankle.

It is concluded that with normal air temperatures the surface temperature of heated floors should not exceed 77° F. or, better, 75° F. (23-9° C.).

A. Garland

1405. The Prevention of Tetraethyl Lead Poisoning in Transport Workers. (О профилактике интоксикации этилированным автобензином у работников автотранспорта)

A. B. REZNIKOV. *Гигиена и Санитария* [Gigiena] 18-23, No. 12, Dec., 1956.

Tetraethyl lead is added to some types of motor and aviation fuel and may act as a cumulative poison among lorry drivers and garage mechanics. The author emphasizes that poisoning by petrol containing tetraethyl lead bears no resemblance to normal lead poisoning nor to poisoning by petrol itself. Its main effects are neurological or psychological, arising from lesions in the cortex, thalamus, and hypothalamus. The usual symptoms are headache, interference with sleep, hallucinations, and asthenia. Later, signs of sympathetic involvement, such as hypothermia, bradycardia, and hypotension may develop, accompanied by tremors of the fingers or eyelids and brisk tendon reflexes. The author points out that it is important to realize that the condition is usually purely subjective, that it may be apparent only when the patient develops some other illness, and that the symptoms of this type of poisoning are common to many, mostly trivial, illnesses. The possibility should be borne in mind, particularly in dealing with transport workers, of confusion between the symptoms of poisoning by tetraethyl lead and those due to carbon monoxide, since the two conditions may occur together.

Investigation of 500 drivers and 100 mechanics and of their working conditions showed that frequently in the repair shops the safe working concentration of tetraethyl lead was exceeded when the fuel system of the vehicles was dismantled. Evidence of subacute poisoning was found in 2 mechanics and 6 drivers, although complaints of headache were more frequent. Subacute poisoning was also found in men who had swallowed petrol when siphoning the fluid from tanks. The author makes several recommendations for avoiding the risk of tetraethyl lead poisoning in these workers. The lay-

out of the workshops should be so planned that work at which the risk of exposure is greatest can be localized to a section of the garage which can be sealed off from the rest and provided with exhaust ventilation. This applies particularly to dismantling the engine and to work on the petrol tank and carburettor. Special precautions are advised for men engaged in cleaning fuel tanks, such as the provision of protective clothing and respirators. The use of the mouth for siphoning petrol must be strictly prohibited. Attention to cleansing of the hands (for which paraffin and dichloramine are advised) is important, and the facilities provided for washing must be good.

Basil Haigh

1406. Hepatic Function in Occupational Carbon Disulphide Poisoning. (Studio della funzione epatica nelle intossicazioni professionali da solfuro di carbonio)

P. CHIESURA. *Minerva medica* [Minerva med. (Torino)] 2, 1945-1949, Dec. 8, 1956. 10 refs.

Examination of hepatic function in 15 patients with carbon disulphide intoxication was undertaken at the Institute of Industrial Medicine of the University of Turin with the object of ascertaining the extent and nature of the liver injury reported, with some variation, by earlier investigators. The methods used included, in addition to clinical examination, estimations of bilirubinuria, bilirubinaemia, erythrocyte sedimentation rate (E.S.R.), and the Takata reaction, performance of the "bromsulphalein" clearance test (which the author considers the most exact estimation of the detoxicating function of the liver), and serum protein fractionation by electrophoresis, which serves to differentiate between parenchymatous and sclerotic lesions of the liver. None of the 15 cases showed either jaundice or splenomegaly, but significant enlargement of the liver was present in 11 and dyspeptic symptoms in 10.

Bilirubinuria was above the normal level in 7 cases, and the serum bilirubin level above 0.5 mg. per 100 ml. in 6 (0.6 mg. in 2, 0.9 mg. in 3, and 1 mg. per 100 ml. in one, in a subject who showed a slight icteric tinge). The Takata reaction was positive in 11 cases, strongly so in 4 of these. The chief abnormality in the serum protein pattern of the 10 persons in whom it was examined was a decrease in the albumin and an increase in the gamma-globulin fractions. Bromsulphalein clearance was significantly reduced in 4 out of 10 cases in which this was determined.

These results, taken together, showed that in all but one case there was some evidence of liver involvement. The lesions appeared to be of two different types—sclerotic in those cases showing disturbance of the serum protein ratios, variation of the Takata reaction, and an increased E.S.R.; parenchymatous (toxic hepatitis) in those with enlarged liver and reduced bromsulphalein clearance. The first type was associated with prolonged exposure to carbon disulphide, the second with more acute and recent exposure. There was no correlation between the results of the function tests and the presence of neurological or vascular injury, but the latter appeared to be of a more serious nature in the presence of the sclerotic type of hepatic lesion.

Ethel Browning

Forensic Medicine and Toxicology

1407. **Toxic Effects and Side-effects of Methylpentynol**
E. MARLEY and J. S. W. CHAMBERS. *British Medical Journal* [Brit. med. J.] 2, 1467-1470, Dec. 22, 1956. 47 refs.

Like many other newly introduced drugs "oblivon" (methylpentynol) has been highly praised; but in view of some recent adverse reports the authors have investigated the potential toxicity and undesirable side-effects of this substance. At the Maudsley Hospital, London, and at Southampton General Hospital, 15 patients were given methylpentynol in doses of 0.5 to 2 g. daily for one to 6 weeks, while 15 obstetric patients received approximately 5 g. of the drug during labour. The following side-effects were frequently noted: dizziness, lightheadedness, a feeling of acceleration of the passage of time, and mild disturbances of body image. A prominent feature was the wide deviation of mood, which ranged from elation and euphoria to irritability, anxiety, tension, apathy, and depression.

The case histories are presented of 8 other patients who experienced toxic reactions after moderate or large doses of methylpentynol. Neurological features of these reactions included loss of tone in the facial muscles, ptosis, ocular paresis, nystagmus, dysarthria, and ataxia. In some cases paraphasia and nominal aphasia also occurred. The psychological features included changes of mood and motor activity, impairment of concentration, visual hallucinations, patchy amnesia, and mild depersonalization. One patient experienced withdrawal symptoms when he stopped taking methylpentynol after 10 months' treatment. The occurrence of toxic effects after relatively small doses is attributed to variations in individual susceptibility to the drug. *Bernard Isaacs*

1408. **The Treatment of Acute Lead Encephalopathy in Children**

J. J. CHISOLM and H. E. HARRISON. *Pediatrics* [Pediatrics] 19, 2-20, Jan., 1957. 5 figs., 19 refs.

The authors, working at the Harriet Lane Home (Johns Hopkins Hospital) and the Baltimore City Hospital, review the results in 36 cases of acute lead encephalopathy in children aged between 15 and 56 months who were treated with sodium calciumedetate (calcium disodium ethylenediamine tetraacetate), and compare them with those in a previous series of 33 similar cases treated with dimercaprol (BAL). The results in the two groups were similar, sodium calciumedetate being no more effective than BAL in terminating the acute manifestations of lead encephalopathy.

The authors seek to reduce the mortality of this condition by earlier diagnosis, prompt removal of the patient from exposure to lead, and careful supportive measures during the first critical 48 to 72 hours of treatment. The dose of sodium calciumedetate used was 75 mg. per kg. body weight per 24 hours given by either continuous intravenous infusion, continuous subcutaneous infusion,

or repeated intramuscular injections in courses lasting 5 to 7 days. The authors have shown that there is a positive correlation between the output of coproporphyrin in the urine and the fraction of the lead in the tissues which is available for chelation and urinary excretion, and they describe how the urinary coproporphyrin level may be used as a guide to therapy with sodium calciumedetate. *H. B. Stoner*

1409. **Lead Poisoning in Children. A Study of Forty-six Cases**

C. D. JENKINS and R. B. MELLINS. *A.M.A. Archives of Neurology and Psychiatry* [A.M.A. Arch. Neurol. Psychiat.] 77, 70-78, Jan., 1957. 2 figs., 3 refs.

In 1953 and 1954 a total of 46 children suffering from lead poisoning were admitted to hospitals in Chicago, 43 of them, it is noted, in the summer months May to September, including 25 in August. There were 13 deaths. The condition was attributed to the ingestion of dried and flaking paint from walls and woodwork in dilapidated houses. Treatment was symptomatic, with administration of calciumedetate in some cases; dimercaprol was not given. Pica was present in 31 of the 32 children who survived. The illness began with signs of cerebral irritation for 7 to 10 days, followed by convulsions, coma, or paralysis. The chief physical after-effects were defects of speech and lack of coordination of the small muscles. After recovery from the acute phase emotional instability, which in some cases persisted for 8 months or longer, and inability to concentrate for more than a very short time were marked. No correlation was found between the lead content or haemoglobin value of the blood and the ultimate outcome. *V. J. Woolley*

1410. **The Direct Coombs Test in Lead Poisoning**

D. A. SUTHERLAND and A. M. EISENTRAUT. *Blood* [Blood] 11, 1024-1031, Nov., 1956. 3 figs., 13 refs.

The result of the direct Coombs test in lead poisoning was studied at the Veterans Administration Hospital and the University of Texas, Dallas. Blood specimens were taken from 20 workers suffering from chronic asymptomatic lead intoxication and from dogs with acute or chronic lead poisoning induced by injections of lead acetate. In all cases there was a positive reaction to the direct Coombs antiglobulin test, which was performed as described by Rosenfield *et al.* (*Amer. J. clin. Path.*, 1951, 21, 301). When the blood was allowed to stand it was found that the cells at the top of the erythrocyte layer had a high percentage of reticulocytes and of cells with basophilic stippling. The reaction to the direct Coombs test was positive in this region, positivity decreasing towards the bottom. Although the result of the test with whole human blood might be negative, a positive result was always obtained for this layer and for whole blood from dogs. *V. J. Woolley*

Anaesthetics

1411. Electrocardiographic Changes in Induced Hypothermia in Man

P. R. FLEMING and F. H. MUIR. *British Heart Journal* [Brit. Heart J.] 19, 59-66, Jan., 1957. 7 figs., 28 refs.

This report is based upon the electrocardiographic findings in 29 of the first 30 operations carried out under hypothermia at Guy's Hospital, London. Lead II was recorded almost exclusively. The ages of the patients ranged from 11 months to 47 years. All the patients showed a progressive bradycardia with fall of temperature, the mean ventricular rate per minute for the whole series being 130 at normal temperatures and 59 at about 28° C. just before circulatory occlusion, but there were big variations—the greatest fall was from 185 to 32, and the least from 88 to 72. Ectopic atrial rhythms associated with a wandering pacemaker, including nodal rhythm, were often seen. Four patients had atrial fibrillation initially; 17 of the remaining 25 developed this arrhythmia at temperatures ranging between 35° and 28° C. The immediate mortality was significantly lower in those who developed atrial fibrillation (29%) than in those who remained in sinus rhythm (75%). Ventricular fibrillation occurred in 21 cases: it usually appeared with little or no warning, and was nearly always related to manipulation of the heart or great vessels, so that the part played by hypothermia in its causation is difficult to assess. Prolongation of the P-R interval was seen in 21 of the 25 patients with sinus rhythm initially, but it exceeded the upper limit of 0.2 second in only 6 of these. Prolongation of the QRS complex was recorded in all but 2 cases, and in 13 of these it exceeded the upper normal limit of 0.11 second. The most striking feature of the electrocardiogram in hypothermia is said to be the appearance of the "injury potential" at the QRS-ST junction. This was seen in 6 cases, and in all but one of these ventricular fibrillation occurred 30 to 45 minutes after its first appearance.

The authors conclude that "the practical value of electrocardiograms in the management of individual patients undergoing hypothermia is not great, but until the metabolic and other changes occurring are better understood, it is clearly valuable to continue to record them for correlation with the clinical condition and prognosis".

William A. R. Thomson

1412. Potassium Depletion and the Central Action of Curare

P. A. FOSTER. *British Journal of Anaesthesia* [Brit. J. Anaesth.] 28, 488-502, Nov., 1956. Bibliography.

This important paper from the University of Liverpool is based on 8 cases in which potassium depletion was associated with an abnormal response to D-tubocurarine or gallamine, and its purpose is to draw attention to circumstances in which curare in clinical doses may produce an apparent central effect. Most of the patients

were suffering from intestinal obstruction, dehydration, and severe metabolic disturbance. Important features of the response included a marked "excitement stage" in which there were struggling and purposive movements after doses of relaxant which would be expected to produce full curarization. This stage lasted 10 to 15 minutes, and thereafter the dose required to maintain relaxation was normal or less than normal. In cases in which potassium loss had been severe and prolonged the effects of curarization could not be reversed with neostigmine and persisted for several hours. Prolonged postoperative drowsiness or unconsciousness, not ascribable to the drugs used for anaesthesia, was an important feature of these cases, and was often accompanied by persistent hypotension.

The hypothesis is advanced that hypokalaemia may permit of abnormal penetration of the antidepolarizing relaxants into the central nervous system, and it is suggested that if this happens curare, which is normally regarded as having only a peripheral action, may have a profoundly depressant effect on the central nervous system. Evidence is advanced that changes in the concentration of potassium and other ions may lead to alterations in the behaviour of biological membranes, so that D-tubocurarine could enter the central nervous system and exert a depressant effect on synaptic activity.

Ronald Woolmer

1413. Trichlorethylene Recondensed. The Implications of a Modification

P. A. FOSTER and U. M. TODD. *British Journal of Anaesthesia* [Brit. J. Anaesth.] 28, 507-511, Nov., 1956. 4 refs.

From the University of Liverpool the authors describe an investigation of the extent to which trichlorethylene vapour may recondense in an ether bottle placed distally to it in the old type of Boyle's anaesthetic machine, given a gas flow of 8 litres per minute and the ether and trichlorethylene control taps full on. The rates of disappearance of trichlorethylene and ether from their respective bottles were noted, temperature readings were taken, and the ether bottle and its J-tube were examined for the presence of trichlorethylene. It was found that with the plungers just covering the openings of the J-tubes, 2.25 ml. of trichlorethylene was transferred to the ether bottle in the course of 2 hours. With the plungers fully depressed, 4 ml. was transferred in 15 minutes, and the J-tube of the ether bottle contained 1 ml. of recondensed trichlorethylene. The authors point out that with the unmodified Boyle's machine there may be some danger that significant amounts of trichlorethylene could be deposited in the soda-lime canister, and there is the added disadvantage that the concentration of trichlorethylene delivered to the patient is unpredictable. It is recommended, therefore, that in any anaesthetic

machine in which a common flow of gases passes through vaporizers arranged in series volatile liquids of lower boiling point should be placed proximal to those of higher boiling point—as is now done in the recently modified Boyle's machine.

Ronald Woolmer

1414. Prestonal. Clinical Trial of a New Relaxant

C. JOLLY. *Anaesthesia [Anaesthesia]* 12, 3-9, Jan., 1957. 2 refs.

There is no known non-depolarizing muscle relaxant which is short-acting and whose action can be reversed by an antidote. Suxamethonium is short-acting, but its effect comes about by depolarization, and of the non-depolarizing relaxants whose effect can be reversed by neostigmine, none has a shorter action than gallamine triethiodide. "Prestonal" is a new muscle relaxant which is short-acting and which has (at least in part) a curare-like rather than a depolarizing effect. It has been reported that its action can be reversed by pyridostigmine, though not by neostigmine.

Working at the General Hospital, Southend-on-Sea, the author has administered the new relaxant on 110 occasions during the induction or maintenance of anaesthesia. Prestonal is structurally not unlike suxamethonium, and 50 to 125 mg. of the dibromide—usually 100 mg.—was given intravenously. The maximum effect began 1 to 1½ minutes after injection. Relaxation was good, but never so complete as that which follows the use of suxamethonium; there was about 3 minutes of relaxation in which to perform intubation. Contrary to expectation pyridostigmine did not reverse the action of prestonal. There were no notable side-effects, and muscle pains after use were less than those sometimes caused by suxamethonium. In two cases there was prolonged apnoea lasting 20 minutes. A wider trial is recommended.

H. Lehmann

1415. Suxamethonium Chloride Administration and Post-operative Muscle Pain

D. B. MORRIS and C. H. DUNN. *British Medical Journal [Brit. med. J.]* 1, 383-384, Feb. 16, 1957. 3 refs.

Although suxamethonium is an excellent muscle relaxant it has the disadvantage of causing in some cases muscle pain and stiffness, occasionally of great severity, in patients discharged from hospital within 48 hours of operation, as first pointed out by Churchill-Davidson (*Brit. med. J.*, 1954, 1, 74; *Abstracts of World Medicine*, 1954, 15, 443). The present authors have therefore studied the incidence of postoperative muscle pain in 229 dental in-patients intubated under suxamethonium chloride (50 to 75 mg.) at the West Middlesex Hospital, Isleworth. The patient's shoulders, chest, abdomen, and legs were suitably exposed in order to observe and record the strength and distribution of fasciculations. Also, each patient was seen and questioned on the day after operation (that is, on the day of discharge), and again 5 days later as an out-patient.

The results were as follows. Some degree of muscle pain and stiffness were complained of by 35% of the patients on the day of discharge, and by 72% on the 5th day after discharge; in 22% of the cases the pain and

stiffness were severe. The authors then tested five modifications of the anaesthetic technique in an attempt to reduce the incidence of after-pains. (1) In 14 cases chlorpromazine was introduced in view of its paralytic action, but no better results were obtained. (2) In 27 cases the suxamethonium was given very slowly and, although the strength of the fasciculations was greatly reduced, no marked reduction of after-pains occurred. (3) In 25 cases 10 to 20 ml. of procaine was given intravenously before induction; this did give slightly improved results, but had to be abandoned on account of the risks of synergism and the time-consuming nature of the technique. (4) In 65 cases D-tubocurarine (5 mg.) was given before induction in the usual test-dose routine; all these patients developed ptosis and, although fasciculations were not entirely abolished, they were markedly reduced. (5) In order to confirm the above result the D-tubocurarine was given in the same dosage (5 mg.), but after instead of before the suxamethonium, in 25 cases; no modification of fasciculation occurred, as expected, since suxamethonium acts more rapidly than tubocurarine.

The authors further noted no determinable relationship between the type of fasciculations and type of after-pains, nor did the nature of the patient's occupation appear to have any specific influence on the occurrence or otherwise of the pain.

[The authors have made a useful contribution to this problem by offering a simple pharmacological antidote which merits further trial.]

Michael Kerr

1416. Respiratory Effects of Anaesthetics. The Effects of Thiopentone, "Nisentil" and Levallorphan on the Respiration

M. SWERDLOW. *Anaesthesia [Anaesthesia]* 12, 42-48, Jan., 1957. 8 refs.

Having already described the effect of levallorphan in antagonizing the respiratory-depressing effect of the analgesic "nisentil" (alphaprodine), the author, in this paper from Salford Royal Hospital, discusses its action on the respiratory depression produced by supplementary doses of thiopentone or alphaprodine given during thiopentone-nitrous oxide anaesthesia. The investigation was carried out on 60 patients who were anaesthetized preparatory to surgery and in whom tidal volume and alveolar ventilation was determined immediately before anaesthesia proper was started. After induction and stabilization on thiopentone-nitrous oxide-oxygen, the patients were given supplementary doses of thiopentone, or of alphaprodine, or of both these drugs preceded by levallorphan.

It was found that, as a supplementary agent, alphaprodine had a less marked effect in depressing ventilation than had thiopentone, although it affected the minute volume more. In the group of patients who received all three drugs there was a considerable depression of alveolar ventilation initially, but within about 15 minutes, although the patients were much more deeply anaesthetized, ventilation was closely comparable to that of patients given one additional analgesic without the antagonist.

Donald V. Bateman

Radiology

1417. The Radiographic Localization of Intracerebral Gliomata

J. W. D. BULL and R. L. ROVIT. *Journal of the Faculty of Radiologists [J. Fac. Radiol. (Lond.)]* 8, 147-157, Jan., 1957. 14 figs., 7 refs.

In view of the importance of accurate location in the prognosis and treatment of tumours of the brain the authors have re-investigated 100 cases of supratentorial glioma which were examined post mortem at the National Hospital, Queen Square, London, between 1947 and 1956; all cases of tumour occurring in the posterior fossa, which have special radiological features, were excluded. Plain films of the skull were examined for signs of increased intracranial pressure and for evidence of lateralization or location of the neoplasm. Contrast procedures were analysed for defining as accurately as possible the precise location of a tumour and the possibility of being able to diagnose its nature from the radiological findings.

It was found that in only 21% of the cases was the neoplasm confined to one specific lobe of the brain. When the neoplasm was in one of the primary lobes of the brain, that is, at a site which might have been regarded as surgically accessible, there was also involvement of deep or midline structures in 64%. Further, one-quarter of all cases showed macroscopical or histological evidence of spread across the midline. In only one case were there two gliomata, in one there was an additional meningioma, and in a third case an unsuspected acoustic neuroma. Of the plain films of the skull, 42% showed signs of increased intracranial pressure. In about one-fifth (23) of all cases the pineal gland could be visualized in the antero-posterior view and of these, 17 (74%) showed a significant shift of the gland to the contralateral side. Of 4 cases in which the examination was repeated at a later date, 3 in which the pineal gland was originally central showed a significant shift at the subsequent examination. Calcification was noted in 3 cases, but this was no evidence as to the size of the tumour. The longest time interval between the last contrast radiographic examination and necropsy was 4½ months, but 89 of the 100 patients came to necropsy within one month.

The presence of a tumour was diagnosed in 90% of all pneumographic studies and 82% of all angiographic studies, but this difference is not regarded as significant. By either method the radiologist could precisely define the exact delimitations of the tumour in slightly less than half of all cases. In the 22 cases in which both air and angiographic studies were carried out the diagnostic accuracy of the two procedures was closely similar. In 71% of all cases in which "pathological tumour vessels were seen within the glioma" the tumour was completely and accurately located, as compared with 47% of all cases examined by angiography. It is con-

cluded that the results of radiography are disappointing in the diagnosis and location of glioma in the early stages of the lesion and that the procedures must be repeated if the neurological signs and symptoms become worse.
John H. L. Conway-Hughes

1418. Congenital Mitral Stenosis. Roentgen Study of Its Manifestations

T. F. HILBISH and R. N. COOLEY. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine [Amer. J. Roentgenol.]* 76, 743-757, Oct., 1956. 11 figs., 22 refs.

A total of 17 cases thought to represent instances of congenital mitral stenosis have been studied roentgenologically in this series. Two of these cases were proved by autopsy. In every instance in which angiocardiology was performed, there was evidence of stagnation of the contrast substance within the left atrium and in every case except one the left atrium was appreciably enlarged.

It appears that congenital mitral stenosis occurs more commonly in conjunction with some associated anomaly than as an isolated lesion. This is borne out by our present series of cases as well as by reports in the literature. Furthermore, recent evidence from our own experience as well as other case reports suggests that congenital mitral stenosis, while still rare, may be more common than previously considered. Finally, it is believed that congenital mitral stenosis can and should be diagnosed by modern diagnostic procedures prior to death. Hence these children may, in selected cases, be afforded an opportunity of a prolonged life by early and skillful cardiac surgery.—[Authors' summary.]

1419. Safe Angiography

J. N. SEGELOV. *Journal of Neurosurgery [J. Neurosurg.]* 13, 567-574, Nov., 1956. 10 refs.

This article describes a safe method of performing carotid and vertebral angiography which was employed at the Royal Prince Alfred Hospital, Sydney, 660 times on 400 patients without any complications or sequelae, apart from a cutaneous rash in 7 patients (1%). The absence of complications is attributed to the small volume of contrast material used and to careful premedication and anaesthesia.

For the first 300 angiograms the contrast medium used was 35% diodone, but this was replaced by 30% "diaginol" (sodium acetrizoate) for the remainder of the series. Both media gave good contrast, but diaginol produced less discomfort to the conscious patient and less stimulus to the anaesthetized. Each view was taken using only 8 ml. of contrast solution. Close cooperation of the radiographer was therefore needed, but the angiograms were equal to, and often better than, those in which larger volumes of contrast substance had been

used. The technique employed for arterial puncture and injection is described in detail for both carotid and vertebral arteries. The solution used for flushing the needle and syringes and keeping them free from clots was a mixture of equal parts of sterile normal saline and 2.6% sodium citrate solution. Up to 120 ml. of this solution could be used without any ill effects occurring.

Premedication is regarded as being very important. In adults this consisted of $1\frac{1}{2}$ grain (100 mg.) of pentobarbitone sodium given $1\frac{1}{2}$ hours before the procedure and $\frac{1}{2}$ grain (20 mg.) "omnupon" with $\frac{1}{10}$ grain (0.44 mg.) of scopolamine 45 minutes before; in children the pentobarbitone was omitted and a suitably smaller dose of omnupon and scopolamine was given. For vertebral angiography 2 grains (130 mg.) of papaverine was given 45 minutes before the procedure in order to lessen the risk of arterial spasm and was found to be of great advantage. Papaverine was also used for carotid angiography in arteriosclerotic patients, but was not found to be of advantage as a routine measure. The anaesthetic to be used was dictated by the patient's state of consciousness and ability to cooperate. This resulted in the use of local analgesia in 272 cases, intravenous thiopentone in 336 cases, rectal "avertin" (bromethol) in 28 cases, bromethol and thiopentone in 21 cases, and ether in 3 cases (young children). Thiopentone was always used for vertebral angiography. The frequency of complications, transient and permanent, and the mortality in other published series are compared in tabular form with those in the present series.

[The author's technique conforms very closely to that used by experienced neuroradiologists in Great Britain.]

J. MacD. Holmes

1420. Angiocardiographic Mixing Defects as Indicators of Left to Right Shunt. [In English]

M. M. FIGLEY, B. NORDENSTRÖM, A. M. STERN, and H. SLOAN. *Acta radiologica [Acta radiol. (Stockh.)]* **45**, 425-437, June, 1956. 11 figs., 13 refs.

From the University of Michigan Hospital, Ann Arbor, the angiocardiographic findings in 3 cases of patent ductus arteriosus together with 3 cases of ventricular septal defect, 2 cases of atrial septal defect, 2 cases of anomalous pulmonary venous drainage into the left innominate vein, and one case of partial anomalous venous drainage into the superior vena cava are described and illustrated.

The authors consider that the observation of incomplete mixing of the opaque medium with the blood in the right heart and pulmonary artery is of value in the diagnosis of left-to-right shunts, though they have noticed that such mixing defects do not occur consistently. They advocate the method of venous angiocardiography, especially when a search is being made for a patent ductus arteriosus. The factors controlling the visualization of mixing defects, such as radiographic technique, projection and timing, the volume of the shunt, and right ventricular pressure, are discussed.

[Altogether this is a very comprehensive review of the subject.]

M. E. Grossmann

1421. Percutaneous Splenic Portal Venography

R. E. STEINER, S. SHERLOCK, and M. D. TURNER. *Journal of the Faculty of Radiologists [J. Fac. Radiol. (Lond.)]* **8**, 158-177, Jan., 1957. 18 figs., 28 refs.

The authors report from the Postgraduate Medical School of London their experience in the performance of the technique of this procedure, which in 39 cases was carried out on the Schonander biplane serial angiographic unit and in 61 instances on a simple cassette tunnel.

With the Schonander table 10 films were taken in each plane in 7 seconds; with the cassette tunnel 5 anteroposterior films were exposed in 12 seconds. Premedication was with 20 mg. of papaveretum and 0.3 mg. of scopolamine, or with amylobarbitone sodium (200 mg.) and pethidine (100 mg.). Local analgesia with 2% procaine was used for adults and general anaesthesia for children. The film should extend above the diaphragm for 3 to 4 inches (7.5 to 10 cm.). The contrast medium was 70% diiodone, of which 40 ml. was injected in adults and 10 to 20 ml. in children, the injection being made at the point of maximum splenic dullness in the mid-axillary line. The needle used, which had an outside diameter of 0.75 mm. and was 7 cm. long, was directed upwards and backwards to be introduced 2 to 3 cm. into the spleen, and was connected by polythene tubing to the syringe. The patients were asked to hold the breath during the actual introduction; blood dripped from the needle when it was within the spleen. The diiodone was injected at the rate of 5 ml. per second and the first film taken after two-thirds of the medium had been given; the injection was usually completed just before the last film was taken. After the examination the patient was kept in bed for 24 hours and the pulse recorded half-hourly.

The indications for transplenic venography are the following.

- (1) Assessment of the portal circulation in patients with portal hypertension and gastro-intestinal haemorrhage.
- (2) To determine whether a portacaval shunt is patent or occluded.
- (3) To determine the cause of extrahepatic portal vein obstruction.
- (4) The elucidation of some cases of unexplained splenomegaly.
- (5) The elucidation of obscure chronic neuropsychiatric disorders in the presence of portal cirrhosis.
- (6) To help in the diagnosis of neoplasms involving the splenic or portal vein.

Contraindications to the procedure are: (1) The presence of severe jaundice even though the patient's prothrombin time may be normal. (2) A one-stage prothrombin time of more than 15 seconds. (3) The presence of ascitic fluid, which must be removed before splenic puncture is attempted. The only serious complication is haemorrhage. To reduce this risk a fine needle must be used and respiration stopped while it is inserted deep into the spleen. Severe pain may be produced by the extrasplenic injection of diiodone, but this is unlikely to last more than an hour. Comparison with other methods showed that oesophageal varices were revealed in 76 patients by venography and in 66 by barium swallow. Comparison of the condition of the portal vein at necropsy with the venographic appearance

in 14 cases showed that there was good agreement in 13. In 8 patients in whom the portal venogram showed no filling of the portal vein it was found on hepatic-vein catheterization that hepatic venous pressure was low. If there is a large collateral circulation which follows mainly one route there may be little if any filling of the portal vein, but such patients are not troubled by haemorrhage and are usually suffering from neuro-psychiatric disorders. *John H. L. Conway-Hughes*

1422. A Review of Trans-splenic Portal Venography in the Investigation of Portal Hypertension. Surgical Aspects

R. M. WALKER. *Journal of the Faculty of Radiologists [J. Fac. Radiol. (Lond.)]* 8, 178-180, Jan., 1957. 2 figs., 2 refs.

Writing from the University of Bristol, the author lays down certain principles which have been found from experience to be of value when considering operation on patients with portal hypertension. (1) That a venous shunt between the portal and systemic circulations is indicated as a means of preventing haemorrhage from oesophageal and gastric varices, but that such a shunt has no place in the direct treatment of ascites. (2) The venous anastomosis must be large; the only adequate veins on the portal side are the portal vein itself and the splenic vein. (3) The nearer the shunt is to the obstruction, the better will it function. (4) Adequate exposure of the portal vein can be obtained only through a right thoraco-abdominal incision. Until 1952 this procedure had one grave disadvantage, namely, that if the portal vein was found to be thrombosed a second incision was necessary; but the introduction in that year of trans-parietal portal venography, by which it could be shown whether the portal vein was patent or not, has solved this problem.

It may be said that in cases of portal hypertension the great value of this investigation is in demonstrating the site of obstruction and the veins which are available for anastomosis. The author has occasionally made use of the investigation in cases of splenomegaly of unknown aetiology, but he has not found it of value in cases of pancreatic disease. The procedure has not been used unless the tip of the spleen was palpable below the costal margin. In 50 cases examined at Bristol there have been no complications. *John H. L. Conway-Hughes*

1423. Intravenous Cholangio-cholecystography with "Biligradin". Its Value as Compared with the Oral Contrast Method

R. W. W. HARDIE and M. ISRAELSKI. *British Medical Journal [Brit. med. J.]* 2, 779-783, Oct. 6, 1956. 1 fig., 28 refs.

The authors stress the fact that although intravenous cholangiocholecystography with "biligradin" is successful as a supplement to oral cholecystography, especially in cases where the oral method has been unsuccessful, it is usually ineffective in the presence of obstructive jaundice or severe liver insufficiency, although its use in such cases is not harmful. It provides an excellent means of demonstrating the presence of stones

in the hepatic and common bile ducts, both before and after cholecystectomy.

They suggest that intravenous cholecystography might be substituted for oral cholecystography as the primary method of investigation, and oral cholecystography reserved for those cases in which it is desirable to assess the concentrating power of the gall-bladder. They also suggest the use of intravenous biligradin as a rapid means of confirming or excluding disease of the biliary tract as the cause of symptoms in abdominal emergencies. *M. E. Grossmann*

1424. Cholangiography by the Biligradin Method with or without Preceding Oral Cholecystography

P. HJORTH. *Radiology [Radiology]* 67, 835-839, Dec., 1956. 20 refs.

Between November, 1953, and January, 1955, the author carried out intravenous cholangiography with "biligradin" at the Copenhagen Municipal Hospital in 270 cases, in 237 of which no gall-bladder shadow had been seen on oral cholecystography, which had been carried out previously in all cases. In 139 cases the gall-bladder was not visualized with biligradin, but a normal common duct was demonstrated. Some of these cases were subjected to operation, which disclosed in one case a calculus of the cystic duct with marked gall-bladder dilatation, in 13 cases inflammatory changes of the gall-bladder with or without calculi, and in 5 cases concretions with no marked changes in the gall-bladder. In 51 cases there was no visible excretion of the medium. In 11 of these cases "the plasma [? bilirubin] values were over 20 [? mg. per 100 ml.]"; in 4 of these a final diagnosis of hepatitis was made and one patient was found at operation to be suffering from hepatic cirrhosis, but in the remainder there were no clinical signs of parenchymal liver disease. In 24 of the remaining 40 cases in this group clinical signs of acute cholecystitis were present, and in 5 cases signs of cholangitis following cholecystectomy, but in the remaining 11 cases there were no clinical signs of cholecystitis or cholangitis.

The author suggests that failure to visualize the gall-bladder associated with successful visualization of the biliary tract following the intravenous injection of biligradin indicates severe changes in the gall-bladder or cystic duct or both, with mechanical obstruction to the entrance of the opaque medium. The oral method is considered to afford more information concerning the function of the gall-bladder, whereas the intravenous method is useful in demonstrating the anatomical structures. *M. E. Grossmann*

1425. Intravenous Cholangiography: Pitfalls in Interpretation

H. S. BERLIN, M. H. POPPEL, and J. STEIN. *Radiology [Radiology]* 67, 840-844, Dec., 1956. 5 figs., 4 refs.

The following pitfalls in the interpretation of intravenous cholangiograms with "biligradin" are emphasized and illustrated by case histories.

(1) Small, translucent gall-stones may be missed, as biligradin often produces a fairly dense shadow, even in a diseased gall-bladder. (2) The sharp edge of the liver,

the renal shadow, loop of small intestine, and the duodenal cap may produce shadows simulating a filled gall-bladder. (3) Biligrafin may be excreted by the kidney, and the renal calyces may be mistaken for the biliary ducts.

M. E. Grossmann

1426. Cholecystography with the Sodium Salt of Iopanoic Acid. [In English]

R. PETERHOFF. *Acta radiologica* [*Acta radiol. (Stockh.)*] 46, 719-722, Dec., 1956. 7 refs.

1427. Roentgenologic Findings in the Stomach and Duodenum in Cancer of the Pancreas. [In English]

K. A. LARSEN and A. PEDERSEN. *Acta radiologica* [*Acta radiol. (Stockh.)*] 45, 459-469, June, 1956. 12 figs., 28 refs.

Over a 5-year period 50 cases of cancer of the pancreas were confirmed at necropsy at Aker Hospital, Oslo, in 31 of which a barium-meal examination had been performed. In 18 cases positive radiological signs for which the malignant condition may have been responsible were found.

From an analysis of these findings the authors conclude that the following findings may contribute to the diagnosis of cancer of the pancreas. (1) Small, smooth impressions and extrinsic pressure defects in the duodenal cap or the second portion of the duodenum. (2) Large defects with destruction of the mucous membrane in the pyloric antrum or duodenum. (3) A widened duodenal loop. (4) Displacement of the stomach and duodenum. (5) Constriction and dilatation in the duodenum. (6) Calcification in the tumour.

M. E. Grossmann

RADIOTHERAPY

1428. Roentgen Treatment of Myeloma with Special Consideration to the Dosage

T. NORIN. *Acta radiologica* [*Acta radiol. (Stockh.)*] 47, 46-54, Jan., 1957. 2 figs., 11 refs.

Cases of myeloma have increased in number during recent years, possibly owing to improved diagnosis. The present investigation was undertaken at the King Gustaf V Jubilee Clinic, Gothenburg, Sweden, to determine the effect of irradiation on local myelomatous deposits and the dosage of radiation necessary to heal them, 30 patients with multiple skeletal deposits, all verified histologically, being studied. Treatment was with x rays generated at 170 to 250 kV with 0.5 mm. Cu + 1.0 mm. Al filter, and was given 6 days a week, the daily dose being 300 to 400 r on the skin. The effect on 53 lesions was assessed by (1) tumour regression; (2) healing of bone destruction; and (3) relief of spinal compression. Strandqvist's fractional diagram was used in recording dosage, the effective tumour dose being reduced to the assumed single irradiation (cumulative dose). This method allows the effects on lesions treated differently to be compared.

Relief of pain occurred in all cases, with objective improvement of 26 lesions and no improvement of 27. There was no objective improvement when the lesion

dose was below 1,000 r. The optimum dose with a high healing frequency corresponded to a cumulative dose of 1,500 r, that is, 3,400 r in 15 days or 4,000 r in 30 days. This dosage should be aimed at in the treatment of all single lesions. When the deposits are diffuse throughout the skeleton those areas which are of greatest danger to the patient should be adequately treated to the same dosage levels.

I. G. Williams

1429. Radiotherapy in the Treatment of Orbital Tumours

M. LEDERMAN. *British Journal of Ophthalmology* [*Brit. J. Ophthalm.*] 40, 592-610, Oct., 1956. 22 figs., 4 refs.

The place of radiotherapy in the treatment of 190 benign and malignant orbital tumours is discussed in this paper from the Royal Marsden Hospital, London. The only benign tumours thought to need radiotherapy are those haemangiomas which do not spontaneously regress or which are in a site exposed to trauma. In these benign cases the results are usually satisfactory and no ocular damage is received. Of the primary malignant tumours, the largest groups are formed by the sarcomata and tumours of the lacrimal glands. Of the sarcomata, those arising from lymphoid tissue are all radiosensitive, but the degree of malignancy varies and is not always consistent with the histology. The prognosis in this group as a whole is good. Of the very rare rhabdomyosarcomata, 7 orbital and 4 extra-orbital cases were seen. The author does not agree with Reese and Duke Elder that these tumours are radioresistant. His experience has been that they are radiosensitive but not "radio-curative", since recurrence took place rapidly. Since these tumours remain localized for most of their natural history delay in exenteration, as a result of trying radiotherapy first, does not appear to add to the risk of metastases. The commonest tumour of the lacrimal glands was the "mixed" tumour, thought to be allied to the mixed salivary-gland tumours. Whatever the histology of these tumours may be, they are considered clinically to be malignant, and radiotherapy associated with surgery is the treatment of choice. Details are given of the various types of secondary tumour encountered, the place of radiotherapy in their treatment, and the results obtained in the whole series are reported.

An extensive account is also given of the risks which the eye undergoes during radiotherapy and the best methods of minimizing damage while at the same time treating the lesion efficaciously. The different parts of the eye vary in sensitivity to irradiation; thus the cornea tolerates it well, provided sepsis and trauma are avoided, while the lens may develop a cataract if a single dose of 600 or 1,500 r in one month is given. Again, differing technical methods produce different degrees of damage. Radon seeds and radium needles usually produce much more severe damage than external radiation. Some protection of the more sensitive structures of the eye can usually be given, but this obviously varies according to the type and site of the lesion. The complications of radiotherapy most likely to occur are discussed, together with indications for their avoidance and reduction when this can be done without reducing also the chance of curing the patient.

V. M. Dalley

History of Medicine

1430. The Hôtel-Dieu de Paris and Its Surgeons (L'Hôtel-Dieu de Paris et ses chirurgiens)

G. MENEGAUX. *Presse médicale* [*Presse méd.*] 64, 2225-2229, Dec. 25, 1956. 5 figs.

The author traces the history of the Hôtel-Dieu in Paris from its reputed foundation in the 7th century, and presents brief annotations on some of its most famous surgeons. Long before the foundation of the Cathedral of Notre Dame the original hospital was housed in three or four small buildings; a charter of the year 829 is extant which calls on the Bishop of Paris to endow the city's hospital. In 1182 these buildings were replaced by others on the right bank of the small arm of the river Seine where it encircles the Ile de la Cité. These, gradually enlarged, were in constant use until the end of the 19th century. In 1505 the administration, hitherto under the exclusive jurisdiction of the Bishop and Chapter, was entrusted to a board of eight Commissioners. The Chapter, however, retained its spiritual function and was expected to care for secular matters in the absence of the administrators. The inevitable conflicts and malpractices are described. In 1652 François Lavocat accorded new regulations to the *Dames Augustines*, their duties to include "service to the sick poor". At this time, also, Vincent de Paul exercised a great influence on the hospital by his organization of the activities of the *Dames de Charité*.

As early as 1221 the surgeon Hubert undertook "in charity and for the repose of his soul" to visit the patients. In the 14th century a regular medico-surgical service was established, and in the 16th century solid surgical studies were ensured by the teaching of the great Ambroise Paré. Fires repeatedly ravaged the hospital during the 18th century, and in 1787 Tenon, finding gross overcrowding, recommended the building of four hospitals on the outskirts of the city. Fortunately, perhaps, the Revolution prevented these recommendations from being carried out. The hospital was rebuilt on the same site and remained there for another century. Finally, under the Consulate, the General Council of Hospitals was created and this system functioned until 1948, when the present scheme of *Assistance Publique* was introduced in France. During the Revolution the need for doctors for the armies led to a radical reorganization of the Faculty of Medicine, which had become completely outmoded, and a report by Fourcroy in 1794 was followed by the creation of "Schools of Health" in Paris, Montpellier, and Strasbourg. The reunion of medicine and surgery under the new Faculty became finally established; Desbois de Rochefort and Corvisart successfully organized bedside teaching of medicine at the Charité and Desault put students through a strenuous and comprehensive course of clinical surgery, without fee, at the Hôtel-Dieu, where Xavier Bichat became one of his most distinguished pupils. On the death of Desault in 1795 the chair of clinical surgery was

filled by Pelletan who became involved in clashes of personality with his young and forceful surgical assistant, Guillaume Dupuytren, whose aim was to extol surgery as a science and to free it from its subordinate status. In the process he quarrelled with Laënnec, Boyer, Richerand, Lisfranc, Récamier, and many others. Since the death of Dupuytren in 1835 the chair of clinical surgery has been held by twelve professors, whose names and dates of tenure are recorded.

Under the influence of the town-planner, Baron Haussmann, Napoleon III transferred the Hôtel-Dieu to its present site on the other side of the great Cathedral square, where it was re-opened in 1878. The author concludes with a plea for the maintenance of this venerable hospital where it now stands in the centre of the city it has served so well and for so long. The crowds of patients daily attending the clinics and seeking admission are a testimony to the respect and affection in which the Hôtel-Dieu is held by the people of Paris.

Norman F. Smith

1431. Mozart's Unhappy Experience of Medicine and Doctors. (Les douloureuses rencontres de Mozart de la médecine et des médecins)

M. PESTEL. *Presse médicale* [*Presse méd.*] 64, 2234-2236, Dec. 25, 1956. 6 figs., 4 refs.

In this survey of Mozart's medical history the author's theme is that, even if the weakling Mozart was threatened from infancy by diseases difficult for him to avoid, it must at the same time be recognized that the medical care accorded him was of poor quality. The life of Mozart was a constant struggle against poverty and there appears to have been a collective culpability on the part of his medical advisers. The infant prodigy, moreover, was overworked by his ambitious father, who failed to secure for him proper medical attention. Eventually Dr Closset, the family practitioner, took pity on him and gave him his devoted, if sadly incompetent, attention.

Certain facts are gleaned from the methodical correspondence of the Mozart family. In October, 1762, the boy, now aged 6, showed the first definite signs of fatigue after a series of strenuous journeys. He complained of pains in the joints, but was not excused from appearing before the Empress at 7 o'clock in the morning. He went to bed on returning home, but no doctor was summoned. Pain in the hip and pelvis was followed by an eruption. Mozart senior, who apparently assumed the role of physician, wrote: "I found . . . spots of the size of a *kreutzer*, red, slightly prominent and painful to the touch. There were only two on the shins and on the elbows. There was some fever". Pharyngeal catarrh was also noted. The author considers this to be a classic picture of erythema nodosum, a condition that was to be described by von Hebra a century later. The following day a Dr Bernhardt saw the boy, spoke of a "kind of

scarlatinal eruption", and paid no further visit. A fortnight later the strenuous touring round Europe was resumed. Thereafter Mozart was frequently laid low by similar attacks, and also suffered from infective articular rheumatism which led to renal damage. In the autumn of 1765 he contracted a fever with a rash; this was deemed to be smallpox, then epidemic in Vienna. However, the illness ran a short and benign course and left no trace, if subsequent portraits are to be trusted.

Mozart himself writes of recurrent illnesses in the course of his journey to Vienna in 1781. An affection of the kidneys is mentioned for the first time in 1784, when he took to his bed for four days, suffering from renal colic with fever and pyuria. It has been suggested that Dr Hunczovsky refused, for mercenary reasons, to attend him. Overwhelmed by debts, the ill-health of his wife, and relentless work, Mozart in 1789 renewed contact with Dr Closset, and it was he who, two years later, attended the composer during his last illness. From contemporary evidence it appears that this illness took the form of renal insufficiency resulting from chronic nephritis. In the summer of 1791 increasing weakness obliged Mozart to slacken the pace. Digestive symptoms, intense headaches, and pallor led the good Closset to diagnose meningitis. Another account of this illness mentions swelling of the hands and feet, while yet another speaks of high fever, shivering, and pleural effusion. On November 28, 1791, Closset called into consultation Sallaba, who gave a hopeless prognosis and visited Mozart on December 5. Mozart died during that night, a few weeks before his 35th birthday.

Norman F. Smith

1432. A Notable Irish Physician

J. D. H. WIDDESS. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] No. 373, 21-31, Jan., 1957.

Thomas Arthur (1593-1675) had probably the largest and most varied medical practice of his time in Ireland. No contribution by him to medical literature is known, although he wrote a treatise on migraine some time after 1654. However, there is a manuscript by Arthur in the British Museum (Add. MS. No. 31885), totalling 285 leaves (probably 375 originally) and containing autobiographical details, historical material relating to his native city of Limerick, accounts of transactions in money and property, and a record of his practice from 1619 to 1666. It is partly in Latin and partly in English, the latter being used for describing financial dealings.

After obtaining the degree of M.A. at the University of Bordeaux, Arthur studied medicine in Paris and then at Rheims, where he received his doctorate, returning to Limerick in 1619 at a time when medical practice in Ireland was not regulated and was carried on by barbers and apothecaries, and by charlatans of all kinds. Arthur's first fee was for curing a case of gonorrhoea, while in his first month of practice he won acclaim for diagnosing pregnancy in a 50-year-old woman. His fame evidently spread, for he was summoned to Dublin, Kerry, and even as far as Dunluce, by members of the nobility. The turning-point of his career came in 1626, when he attended and cured Archbishop Ussher of a mysterious

affliction which had baffled the King's physicians in England. As a result Arthur, although a Catholic, was appointed physician to the Viceregal household. In 1630 he found it necessary to take up permanent residence in Dublin, where, as his record shows, he attended patients of all social classes. When the civil wars began in 1641 he returned to Limerick. Here his royalist sympathies brought him a term of imprisonment and heavy fines levied by the Parliamentary forces. Nevertheless he was able to return to Dublin in 1652, where he won the confidence of the Parliamentarians, including Fleetwood, who ruled Ireland in the name of the Protector, and Henry Cromwell, Oliver's brother, who became Lord Deputy. His practice, however, was never as prosperous as formerly.

Arthur's manuscript shows him to have been a skilful physician, and one who, although patronized by the wealthy classes, did not scorn the humble. He won respect from all, including religious and political opponents. His erudition is manifested in his Latin verses, which he appears to have composed with ease, and in the scope of his library, which contained, besides 152 medical books, another 160 covering logic, dialectic, rhetoric, philosophy, metaphysics, history, architecture, astronomy, religion, and the Latin classics. Arthur seems to have retired from practice in 1666.

Geoffrey R. Pendrill

1433. The Pernicious Remedy of the Naval Surgeon

J. DOBSON. *Journal of the Royal Naval Medical Service* [*J. roy. nav. med. Serv.*] 43, 23-28, 1957. 1 fig.

"The pernicious remedy of the Naval surgeon" was tobacco. In the Charter granted by Charles I to the Company of Barber-Surgeons in 1629 a clause was inserted requiring that the surgeon on any ship leaving the port of London was to have his instruments and medical equipment "examined and allowed by two of the Governors of the Mystery". In spite of several attempts to change this regulation the privilege was closely guarded, but in 1800 the clause was included in the Charter of the Royal College of Surgeons. In 1812 the Court of Examiners was asked to revise the list of instruments "required to be provided by surgeons in the Navy". The court made a few alterations, the most interesting of which was the recommendation that there be omitted "that portion of the apparatus for the use of the smoke of tobacco in the case of suspended animation because, tobacco in such case, howsoever employed, so far from animating, must always have a deadly tendency".

A brief history is given of the use of tobacco as a remedy for many ailments and of its unfortunate adoption by the Royal Humane Society. John Hunter, who was a member of the Society, wrote cautiously about the use of tobacco: "I would avoid likewise throwing anything in by the anus which might lead to an evacuation that way, as every such evacuation also tends to lessen the animal powers; of course, I have avoided speaking of the fumes of tobacco which always produce sickness or purging according as they are applied." In 1811 Benjamin Brodie showed by experiments on animals that tobacco had a poisonous effect. Zachary Cope

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